ALLOPLANT - THE GENERATION OF TRANSPLANTS FOR EYES AND PLASTIC SURGERY


The new in essence kind of transplants for eyes and plastic surgery trade marked as "Alloplant" has been worked out by physical and chemical reconstruction of collageneproteoglycam complex. The unique features of these new transplants are low antigen activity and the ability to replace alloplant by the recipient's own tissues (regenerator) after transplantation. The structure and the features of regenerate can be regulated by choosing from the different kinds of alloplants. In the authors clinic different kinds of alloplants are produced for eyes and plastic surgery, stomatology and neurosurgery, traumatology and proctology.

ALLOPLANT SCLERAL REINFORCEMENT IN PROGRESSIVE MYOPIA


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Progressive myopia is one of the main causes of blindness. Among the causes of blindness, myopia takes 5.6% in USA [4], 6.6-14.7% in Germany [8], 24% in Russia [7]. Various methods of progressive myopia treatment proposed by different authors do not control progression of myopia.

It appears rather prospective to further develop the technique of scleral reinforcement that was worked out earlier [1, 2, 16 19,9 etc.], since this is the only method that controls myopia progression. However, the method of scleral reinforce-ment is not widely applied in ophthalmologic practice as long as it entails numerous complications, such as retinal detachment, hemorrhage into the retina and vitreous body, compression of the optic nerve, uveitis, glaucoma etc., which were documented in 7-27.5% of cases [3, 9, 20].

We began performing reinforcement surgeries in 1979 using i-shaped allografts of donor sclera by the technique of A.Snyder and F.Thompson [19]. The first 15 procedures were successful, but in the 16th case a severe surgical failure took place when vitreal hemorrhage, optic nerve atrophy and retinal detachment were diagnosed postoperatively. The visual acuity went from 0.6 down to 0. Apparently, the cause of this failure was compression of the optic nerve and blood vessels due to the lack of visibility during the surgery. Topographic analysis of this failure showed that the strip of donor sclera may compress not only blood vessels in the posterior aspect of the eyeball, but also the optic nerve, particularly in those cases when the optic nerve approaches the eyeball slantwise.

Also, allografts of donor sclera have obvious drawbacks, such as severe inflamma-tory reaction [18] and excessive scarring around the graft [21]. Purposes of research:

1. To develop a new graft for scleral reinforcement;
2. To develop a new surgical technique of scleral reinforcement;
Fig. 1

Fig. 2
Dynamics of axial length in Alloplant scleral reinforcement (450) years

<table>
<thead>
<tr>
<th>mm</th>
<th>Initial refraction</th>
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<tr>
<td>25.0</td>
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<td>25.5</td>
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<td>28.0</td>
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- -6.0
- -6.0-10.0
- >10.0

pre-op 1 3 5 7 7-13 years

Mean difference from pre-op: *-p<0.05
Fig. 3  Dynamics of refraction in Alloplant scleral reinforcement (450) years

Diopters

Initial refraction

- -6.0
- -6.0-10.0
- -10.0
- Total

pre-op 1 3 5 7 7-13 years

Mean difference from pre-op: * - p<0.05
** - p<0.01

Fig. 4  Gradient of myopic progression (cluster analysis) (450 eyes)

Diopters change

-2.5 -2.0 -1.5 -1.0 -0.5 0.0 0.5 1.0 1.5

pre-op 1 3 5 7 7-13 years

Ordinate: mean of annual refraction increase
Fig. 5
Dynamics of visual acuity (corr.) in Alloplant scleral reinforcement (450) years

Initial refraction:
- -6.0-10.0
- <=-6
- >=-10.0
- - Total

Vis

pre-op 1 3 5 7 7-13 years

Fig. 6
Dynamics of Visual Acuity (corr.) cluster analysis, 450 operated eyes

Vis

pre-op 1 3 5 7 7-13 years

2 3 5 4 1
Fig. 7  Dynamics of visual acuity (corr.) in Alloplant scleral reinforcement (450) years

Fig. 8  Dynamics of dystrophy pattern on initial retinal dystrophy (multiple regression analysis, 450 eyes)
Development of a new graft for scleral reinforcement

Considering the literature data and our own experience about the drawbacks of donor sclera, we tried to find another grafting material for scleral reinforcement. We turned to "alloplant" - a new type of implants produced from human cadaver tissue. These allografts, developed in our institute 17 years ago [10,11, 12, 13, 14] have the following basic features:

- low antigenicity, attained through the change of correlation between glycosaminoglycans and collagen fibers in the processed tissue;
- prevention of scarring around the allograft, attained through a special principle of tissue selection;
- selectable growth of host tissues during replacement of alloplant, attained through changing the content of glycosaminoglycans in the graft.

Using the above principles of attaining the specific features, we produced an alloplant for scleral reinforcement. This implant is prepared from human cadaver fascias (lamina superficialis f.thoracolumbalis) and tendons (tendo m.latissimi dorsi) by Alloplant Production Laboratory (Ufa, Russia). The process of alloplant production includes morphometric selection of tissues, chemical treatment under histochemical control, histochemical selection of tissues, a number of control steps (polaroid-optical, byomechanical, histological, bacteriological, AIDS- and HBV-tests) and sterilization by irradiation. Alloplants preserved in 70% ethyl alcohol can be stored for over 5 years at room temperature.

Experimental research into application of alloplant for scleral reinforcement was carried out in 54 rabbits, donor sclera being used as control. Of all rabbits, 27 were operated on with the use of sclera, 27 with donor rabbit sclera. Patches of allografts (7x7 mm) were sutured to the sclera in the equator area. Post-operative histological examinations were carried out at 7, 14, 30, 90, 180, 360 days after surgery. The methods of morphological examination included hematoxylin-eosin staining, Van-Giezon staining, naphthol green staining, Mallory staining, Suzuki-Sekiyama silver impregnation, polariza-tion microscopy, transmissive electron microscopy, scanning electron microscopy.

In the early period (7-14 days) after implantation of donor sclera, severe inflammatory reaction was found: infiltration of lymphocytes, neutrophils, macrophages, fibroblasts as well as pronounced edema of the graft and swelling of collagen fibers. In the same period, the cases with alloplant showed slight inflammation: not-excessive infiltration of macrophages and fibroblasts, scattered lymphocytes and neutrophiles as well as insignificant edema of the graft. Evaluation of tissue
reaction according to Sewel (1980) revealed more pronounced reaction after implantation of donor sclera versus alloplant. It was shown that implantation of donor sclera provoked strong humoral and cellular immune response to tissue antigens. In contrast, alloplant-operated rabbits no immune reaction was observed.

At 30 days, inflammatory reaction persisted in the cases of donor sclera and, in the cases of alloplant, subsided as fibroblasts grew in.

At 90 days, incipient incapsulation and scarring around the donor sclera was found. By this time, the alloplant contains numerous proliferating fibroblasts and newly-formed collagen fibers following the rows of fibroblasts, slight infiltration of macrophages, no incapsulation or scarring around the alloplant are present.

At 180 days, incapsulation and scarring around the donor sclera is evident. In the cases of alloplant, the process of replacement thereof by a sclera-like tissue continues, the alloplant closely adheres the recipient sclera.

At 360 days, the donor sclera grafts have deformations, cicatricial changes, severe scarring and the graft does not adhere to the recipient sclera. In the cases of alloplant, the replacement of the graft is mostly finished; the newly-formed tissue that replaced the graft is of compact texture, there is no border between the regenerate and host sclera; thus, thick sclera is formed. Scanning electron microscopy shows rough and uneven surface of the donor sclera as compared with rather smooth surface of the tissue that replaced the alloplant.

**DEVELOPMENT OF SURGICAL TECHNIQUE**

During the work upon surgical technique of scleral reinforcement, 2 points were taken into account: myopic sclera stretching in various areas of the sclera and topography of the vortex vein.

According to the literature [3, 20], the majority of stretching areas in high myopia are the posterior or temporal sectors. A byomechanical study of donor sclera with the use of the breaking machine ZM-100 revealed more elongation in the posterior-temporal region than in the posterior-nasal one (0.20 versus 0.17). Thus, scleral reinforcement in progressive myopia is more reasonable in the posterior and temporal areas of the sclera.

We studied the topography of the vortex vein in 14 human cadaveric eyes after postmortem injection of Paris blue and read lead. Dissection of the Tenon’s capsule revealed that, as a rule, 4 vortex veins are present, which lie in the following areas: under the inferior rectus, in the inferior-medial sector, under the medial rectus and in the superior-medial sector. The obtained data conform to the findings of B.Curtin [2].

Since we could not find vortex veins in the temporal area of the sclera by the post-mortem examination, we carried out clinical research on vortex veins in the temporal sector of the sclera during 300 surgeries (scleral reinforcement, choroid revascularization etc.). Only in 1 of 300 cases (0.3%) a vortex vein was found in the tempo-ral area.

Therefore, scleral reinforcement performed in the posterior-temporal area of the eyeball is the most safe and effective.

Mathematical calculation of the graft shape, the anatomical features of this area (muscles, vessels) being taken into account, permits the elaboration of a special shape of the graft (fig.1). The graft of such shape fixed to the sclera with 4 sutures exerts three pressure areas:

a) high pressure area in the equator area, where no vessels are found;

b) moderate pressure area around the inferior oblique, where no vessels are found;

f) low pressure area in the macular area and around the optic nerve where the posterior ciliary arteries lie. The latter are not compressed by the graft due to the low pressure.

**SURGICAL TECHNIQUE**

The surgery is performed under local or biauricular or general anesthesia (basing upon the age of the patient).

A conjunctiva incision is made in the exterior quadrants of the eyeball over the fixation line of the rectus muscles (parallel to the limbus). Guy-sutures are placed on the exterior rectus, inferior oblique and the conjunctiva. A transplant with a fenestration for the inferior oblique (4-5 mm in diameter) and an indentation for the optic nerve, is placed around the fixation point of the exterior
rectus, then guided under the exterior rectus and fixed ahead of the inferior oblique and along the equator (on the fixation line of the rectus muscles) with four interrupted episcleral sutures. Thus, the transplant covers the upper and lower exterior quadrants and the posterior aspect of the eyeball around the optic nerve, being placed under full visual control. A continuous suture is placed on the conjunctiva.

Indications for scleral reinforcement surgery are cases of progressive myopia with annual progression rate of 1 diopter and over, with annual elongation of visual axis over 25 mm or with advanced fundus pathology.

In post-operative period the patients were locally administered desinfecting drops. The sutures were removed at 5-7 days after surgery.

The response of the adjacent tissues to surgery was estimated according to the system used in Russia (Malysheva T. P., 1985). The weak degree of reaction was found in 87.2% of patients, medium in 12.8%, which subsided in 1-5 days. We couldn’t observe any specific immune reaction in alloplant operated patients, using passive hemagglutination and migration inhibitory tests. There was also no changes in lymphocytes subpopulations (CD3+, CD4+, CD8+, CD12+) during postoperative period.

Over 6000 scleral reinforcement surgeries have been performed with the use of the mentioned technique. The results of 1500 surgeries were reported at the 4th International Conference on Myopia (Singapore, 1990). In this work, randomized analysis of 280 patients (450 eyes) is being presented. The age of the patients ranged from 3 to 50 years (21.12 ± 7.01). Refraction ranged from -1.75 to -33.0 diopters (-10.85 ± 4.19). Visual axis ranged from 25 to 34 mm (27.24 ± 1.67). Before surgery, the patients were observed for 1-3 years. During this time, refraction de-creased by 1 to 4.5 diopters (1.55 ± 0.69). The mean age of myopia start was 8.39 ± 3.02. The mean duration of myopia before surgery was 12.81 ± 7.3. Dystrophic fundus change was 1.47 ± 0.65 points. The mean interval between surgeries on the right and left eyes was 5.27 ± 4.84 months.

The patients were examined before surgery and at 1,3,5,7,7-13 years after surgery: visual acuity (with and without correction), clinical refraction, axial length, visual fields (total of 8 meridians with the use of Goldman's perimeter, stimulus IV-4) were determined. Patients with high axial and complicated myopia were given prophylactic laser coagulation before surgery. Reinforcement of the exterior quadrants and the poste-rior aspect of the eyeball was carried out in alt patients. As is usually done, the first surgery was performed on the eye of worse vision.

The data were processed with the use of multivariate statistics (multiple regres-sion, cluster analy-sis) as well as standard univariate statistics.

For analysis of the results of the surgeries, the patients were divided into groups as to the following initial parameters: refraction - (1) up to -6.0 DPTR, (II) -6.25..-10.ODptr, (III) over-10.25 Dptr: duration of myopia-(1) up to 9 years, (II) 9.1-15 years, (III) 15.1-47 years; degree of dystro-phy - (1) I degree, (II) 11-111 degree, (III) IV-V degree.

RESULTS & DISCUSSION

The analysis of axial length dynamics showed the absence of statistically sig-nificant changes in the groups with different initial refraction (fig.2) over the control period, with the exception of the patients with initial refraction of below -6 Dptr which presented a confident decrease of axial length at 5 years after surgery. Myopic refract-ion during the same period increased by 0.63 diopters on the average (fig.3). Consider-ing that the annual refraction increase was -1.56 Dptr, stabilization of this parameter can be stated. However, the dynamics of refraction in different initial refraction groups was substantially different. Thus, in group (below -6 Dptr), a significant refraction increase of 2.45 Dptr was stated at 7 years. An abrupt decrease of myopia progression was also found by cluster analysis (fig.4), in which case this decrease was most pronounced in the clusters with initially high progression rate.

Visual acuity with correction (fig.5) reliably increased in all groups at 17 years after operation and was reliably higher at the end of observation in group (over-10 Dptr). Stabilization of visual acuity in the groups with initially high values and increase thereof in the groups with initially low values is also confirmed by dynamical analysis of the cluster groups.

As the data show (fig.6), the increase of visual acuity after surgery is mostly found in the groups with moderate and high degree of retinal dystrophy. Likewise, axial length and myopic refraction changed primarily in the patients with dystrophic fundus changes. Calculations of linear correlation demonstrated a high link between initial retinal degree and initial values of all measurable param-
eters: from -0.84 to -0.89 for visual acuity, visual fields and refraction; and up to 0.86 for axial length. This allowed us to theoretically calculate the dynamics of retinal dystrophy after surgery (fig.7). The points on the curves correspond to the equation (1) in the cases of different initial retinal dystrophy.

\[ DP=1.73+(-1.6*VA)+(-0.02*R)+(-0.03*AL)+(-0.0006*VF), \]  
where, DP- dystrophy pattern, VA- visual acuity, R- refraction, AL - axial length, VF -total of visual fields by 8 meridians.

The presented data demonstrate a rather high efficacy of scleral reinforcement with the use of Alloplant and the proposed surgical technique. Judging from the stabil-ity of most control parameters, this operation ensures stabilization of the myopic process within the observation period. The stabilization of axial length and refraction, apparently, can be accounted for by the enhancement of the biomechanical properties of the sclera due to the regenerate that replaces the alloplant and has the quality of close adherence to the sclera. At the same time, the results of the analysis convincingly demonstrate the halting and reduction of dystrophic processes in all groups of patients. This effect contin-ues for 7 years after operation, in the least, and can probably be accounted for by the increase of ability for visual acuity correction in the treated eyes (fig.8). One the possible mechanisms of this effect, to our opinion, consists in excreting physiological active substances by proliferating cells (mostly, by fibroblasts of different generations) in the place of the replaced regenerate, particularly different cytokines that control the growth, differentiation and other cellular responses. According to [5,6], the basic fibroblasts growth factor and, to a less degree - cytokines, substantially inhibit degeneration of photoreceptors and pigment epithelial cells in RCS rats and animals with experimental photodegeneration of the retina. It is worth noting that, according to our data, the process of alloplant replacement lasts for not less than 5 years and during this period, in the least, the influence of the mentioned substances on the retina can be expected.

REFERENCES

NEW TRANSPLANT FOR SCLEROPLASTY IN MYOPIA AND ITS EFFICIENCY IN 1,500 OPERATIONS

Dr. Muldashev E., Dr. Bulatov R., Dr. Rodionov 0., Dr. Salikhov A., Dr. Muslimov S.

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Allotransplant had been selected as a single block with eye-ball. On the 3rd day band- fibrous structure of allotransplant was completely preserved. The most peculiar thing is the strengthening of argentophylia of fibrous bands and prolapse of separate cores of silver in impregnation of preparations by V.V. Kuprianov. Distinction of cellular elements of a transplant- nuclear dentionation and deformation, wrinkling of cytoplasm. Insignificant macrofagal- fibroblastic infiltration of surrounding tissues, primarily in the field of suture fixation. On the 7th day along with preserving For the last time one of the most effective methods of treatment of progressive myopia are sclero-strengthening opera-tions (Avetisov E.S., 1931).

The use of wide thigh fascia as plastic material of Y & X - sclero-plasty in progressive myopia promotes stabilization of the process in 95% of operated patients (Nesterov A.P., Libencon N.B., 1976), sclera- for intralamellar scleroplasty-in 96,1% (Panfilov N.J., 1977), sclera- for sectoral scleroplasty- 88% (Zaikova M.V., Mazchenko V.P., 1979), dura mater accord. to Pivovarov’s method-87,3% (Pospelov V.J., 1937), at the same time transplant gives stabilization of the process in 38,7% of cases (Butiukova V.A., Rosliakova A.G., 1937).

Such a great difference in showings of Myopia stabilization, described by many authors, is the result of absence of the single method of the results accord. to degrees and development of myopia, varied from the age of patients, unequal term of follow-up observation (from 0,5 to 7 years) and other com-ponents.

Allotransplant for sclera is widely used (Kagermazova N.V., 1975). But the application of this transplant is restricted by its small anatomical structures and difficulty of tissue selec-tion from dead eyes because of national- religious traditions. Dura mater (Khatminsky Y.Ph., 1986), amnion (Zaikova M..A., 1983), wide fascia of thigh (Adygezalova- Ponchaeva K.A., 1984) have more large structures, and because of friable many-oriented position of collagenic structures in the process of sub-stitution in transplantation, in its place there is formed a friable regenerabor with less sclero-strengthening effect.

The aim of this publication is the investigation of sclerostrengthening effect of the new allotransplant "Alloplant", elaborated in Ufa’s laboratory of transplants for ophthalmosurgery MNTK "Eye Microsurgery" in case of progressive myopia, and it depends on the degree, character of growth, the age of patients, and complications.

Using this transplant, we issued from the fact that accord. to biomechanical properties tendons are the most firm, elastic and indifferential transplants in immunological meaning (Obusov A.S., 1971; Sorokin A.P., 1973). The latest in allotransplantation are well used and substituted by dense connective tissue, which can fulfill the fixative function (Efimov A.P., 1976).

The conducted biomechanical investigations on the material of 38 corpses showed the high firmative properties of the given transplant- Q = 19 - 20 kgs/mm2; in comparatively small de-formative possibilities E = 0,14- 0,22; high indices of density module - E = 91- 159 kgs/mm2. For comparison it is possible to give the same indices for wide fascia of thigh - Q = 8- 16 kgs/mm2. This "stock of density" is especially important for transplants in fixative and strengthening operations.

Besides, lamellar structure, optimal thickness 0,8 - 1,0 mm sufficient optional square in- 120 - 180 cm2; two - layeredfirm dislocation of connective tissue structures in the angle towards each other