HISTORIC SURVEY OF POSTERIOR LAMELLAR KERATOPLASTY TECHNIQUES – AN OVERVIEW

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SUMMARY

Some of the modifications of posterior lamellar keratoplasty is at the present considered by most of the corneal surgeons as method of choice in case of patient's corneal endothelium damage. However, this surgical technique undergoes in the last 20 years relatively rapid development. Even in the current time, there exist side by side and are used different types and modifications of this sort of transplantation. Because of this reason, differences among individual methods are sometimes not accurately understood and the terminology may be used not exactly as well. The authors specify all until now described surgical methods, describe differences among single surgical procedures, and point out their advantages and disadvantages. The methods are described in the same order as they were historically introduced into the literature.

Key words: posterior lamellar keratoplasty, surgical methods

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INTRODUCTION

Dysfunction of the corneal endothelium remains one of the most common indications for the performance of one of a number of types of corneal transplant. Disorders of the function of the endothelium, such as bullous keratopathy (BK), Fuchs' endothelial dystrophy (FED), posterior polymorphous dystrophy of the endothelium (PPD) or other types of dystrophies are the surgical diagnosis for example in 42.1% of performed transplants in a Columbian study (17), 35.8% in a German study (63), 30.3% in a Scottish study (59) and 31.1% in a long-term observation in Hungary (39). In the national register of corneal transplantation in Australia it is stated as 31.8% of these indications (64) and in New Zealand 22.3% (12). In the Czech Republic, in 2012 40% of transplants were performed due to BK, 16.1% due to Fuchs' dystrophy, in total 261 (56.1%) of transplants (51).

From 1905, when Eduard Zirm performed the first successful perforating keratoplasty (PKP) operation (65, 66), up to the end of the 20th century, this operation was the only known option for the effective treatment of failure of the corneal endothelium. Although PKP is a very effective method of corneal transplantation, it nevertheless does not differentiate the structures of the cornea which are afflicted and responsible for deteriorated visual acuity. In the case that the indication for transplantation is damage to the stroma (or if applicable other parts of the anterior layers of the cornea), healthy corneal endothelium is sacrificed in PKP. Conversely, in the case of dysfunctions of the endothelium, during the course of PKP layers are removed which are not afflicted, or only secondarily and as a rule reversibly afflicted (edema of the epithelium or stroma). The removal of these relatively healthy layers of the corneal stroma causes irreversible loss of the normal corneal topography and impairment of the structural integrity of the anterior parts of the corneal tissue. PKP is furthermore burdened with a whole range of potential perioperative and postoperative complications. The most frequent complications occurring during the course of surgery include primarily damage to the tissues of the anterior segment (iris, lens), loss of vitreous body and haemorrhage. Probably the most serious, sight-threatening complication is expulsive choroidal haemorrhage. In a group of 2421 patients with performed PKP, Groh states the incidence of pre-expulsive haemorrhage in 9 patients (0.4%) and expulsive haemorrhage in 3 patients (0.1%) (20).

Also during the course of postoperative healing of patients following the performance of PKP, a relatively high percentage of complications is described. Not only the actual healing and the presence of corneal sutures, but also the necessary long-term local steroid therapy is connected with certain further potential complications such as the incidence of secondary glaucoma, complicated cataract or infectious inflammations. In a group of 910 performed PKP operations, Wagoner states the incidence of at least one postoperative complication in 362 eyes (39.8%). The most frequent complication stated is endothelial rejection (17.3%), followed by secondary glaucoma (15.5%), bacterial keratitis (5.8%), persistent epithelial defect (3.4%) and dehiscence of the wound (1.6%) (62). In another study Farjo states the number of rejections following performed PKP for BK at 9.8% over the course of an observation period of 36 months (16). Other relatively frequently stated complications include: increase of intraocular pressure in 42% of patients following PKP (6), incidence of microbial keratitis in 12.1% of patients in a group of 323 PKP (26) and 7.4% in a group of 285 performed keratoplasties (3). More rarely stated complications are ingrowth of the epithelium (4) or dehiscence of the wound in 2.53% (60). One of the most serious postoperative complications, which may lead to functional loss of the eye, is endophthalmitis. Taban evaluated pub-

lished studies describing the results in a total of 90 549 eyes with PKP, and recorded an incidence of postoperative endophthalmitis at 0.382% (54). In the Czech Republic Jirásková et al. described the frequency of complications following PKP in a smaller group of patients. In a group of 100 performed PKP with an average observation period of 10 months they state a rejection reaction in 23% of eyes, endophthalmitis in 4.1% and increased intraocular pressure in 5.4% of eyes (29).

With regard to the above-mentioned risks in connection with PKP, ophthalmic surgeons have sought a way to replace only damaged corneal endothelium, or the endothelium, Descemet's membrane (DM) and deep layers of the stroma. Probably the first description of such a procedure in the professional literature appeared in 1956, when Tillet published his study Posterior Lamellar Keratoplasty. Following the creation of a non-perforating, 180 degree incision in the periphery of the cornea, the cornea was divided throughout its entire scope into two lamellas. After the removal of a superficial flap comprising one half of the cornea, deeper layers were extracted using forceps, a donor lamella was stitched onto the limbus of the recipient using a U-suture and stitched over with the superficial lamella of the recipient. The author presented this technique in the case of one patient whose cornea was clear one year after surgery, nevertheless a loss of vision occurred due to glaucoma (58). In the 1960s methods of replacement of the endothelium via an anterior pathway following the creation of a corneal flap (in situ keratomileusis) were described by José Barraquer (9).

In 1998 a new method of posterior lamellar keratoplasty was described by Gerrit Melles (38). The afflicted endothelium, including the DM and deep layers of the stroma were removed from the eye of the recipient following separation of the cornea by an approximately 9 mm tunnel sclerocorneal incision. Using special curved sharp spatulas (fig. 1) the recipient's cornea was separated practically throughout the entire scope from limbus to limbus. A lamella was created in the deepest possible layers of the stroma and was estimated by the surgeon by means of a visual check. For this purpose air was injected into the anterior chamber, and optic phenomena produced on the cornea-air interface were used, primarily the reverberation of the tip of the instrument and the drape of the DM. By this method it was possible to attain a separation in approximately 90-95% of the depth of the stroma. The created deep lamella from the eye of the recipient was cut off using 3 forceps of various curvature (fig. 2). By the same method the lamella from the cadaverous donor bulb was prepared, only trepanning was performed by punch from the endothelial side following cutting of the cornea from the bulb. The thus created donor lamella was implanted using forceps or on a metal or plastic support, and fixed in the eye with the use of an air bubble. The fact that the use of suturing is not necessary for the fixation of the lamella is a further substantial benefit of this method, and this technique is used in all subsequent types of operations. This technique of posterior lamellar keratoplasty was further developed by Terry and Ousley, who also renamed it Deep Lamellar Endothelial Keratoplasty (DLEK). These authors proposed the preparation of a donor lamella from a cornea located on an artificial anterior chamber, which also represented a simplification of the entire method and enabled the use of a cornea supplied by tissue banks (56), whereas previously

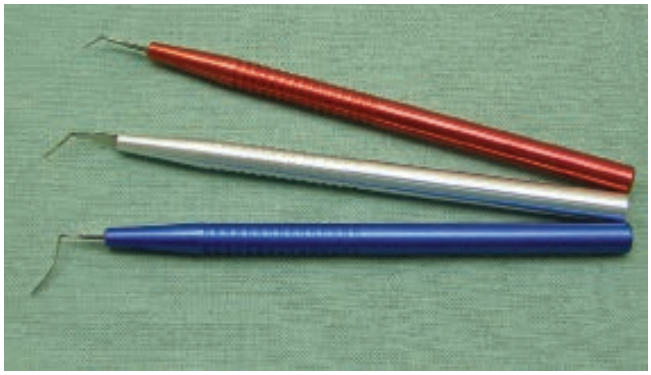

Fig. 1 Sharp spatulas used for dividing the cornea in DLEK and DSEK type operation

Fig. 2 Forceps used for removing deep corneal lamellas of the recipient in DLEK type operation

the procedure had required preparation from the entire enucleated bulb of the donor. A modification of the DLEK technique was implantation of the lamella in folded state (fig. 3), in which its spontaneous unfolding and subsequent fixation by air took place in the anterior chamber. By this method it was possible to reduce the surgical wound to approximately 5 mm, and perform the entire procedure without suturing (37). First of all forceps were used for the actual implantation, nevertheless at present there are a whole range of techniques, it is possible to use one of the types of commercially available instruments such as a Busin

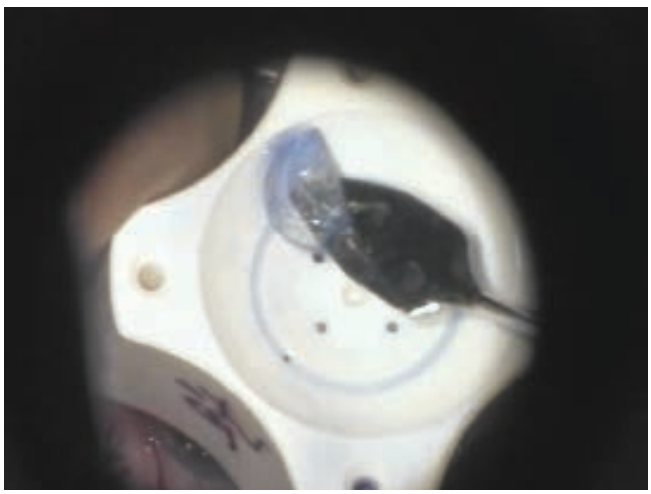

Fig. 3 Transfer of folded lamella of DSEK type

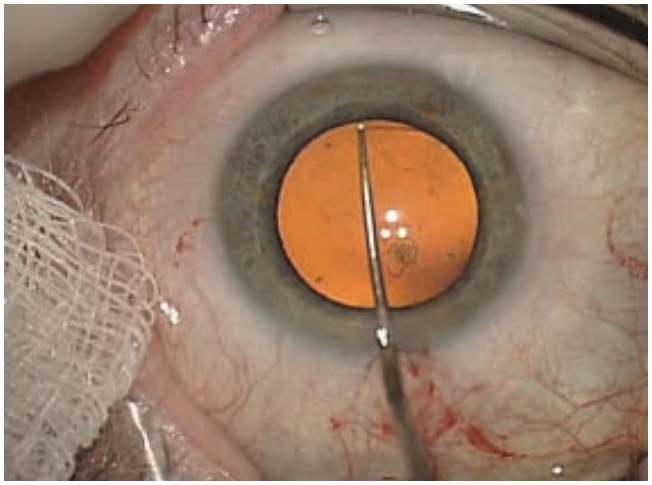

Fig. 4 Descemetorhexis

glide, Tan endoglide etc. Further methods of implantation of the lamella have been described, for example drawing the lamella into the anterior chamber with the help of a suture (30), hydro -implantation with the use of a plastic cartdridge etc. In any case, implantation of a lamella in a folded state and performance of surgery with a small incision is currently the standard method of implantation in all types of lamellar endothelial transplants. With regard to the considerable surgical difficulties of the DLEK technique, however, this method spread only to a relatively small extent, nevertheless it prefigured the arrival of further techniques of endothelial replacement. In 2015 Alió Barrio published a modification of this technique, in which he used a femtosecond laser for separation of the cornea. The authors state that a thus performed DLEK type operation may be the method of choice even at the present time, for example in cases where, in addition to the endothelium, deep layers of the recipient's stroma are also damaged and turbid (5).

In 2003 Sinha described a new technique for removing the DM from the patient's eye – descemetorhexis, in which the DM is relatively simply peeled with the help of a surgical hook (50) (fig. 4). This technique was first used by Melles (36) and Price (45) as preparation of the recipient's cornea in endothelial keratoplasty. The technique was named DSEK (Descemet Stripping Endothelial Keratoplasty). All the subsequently published surgical procedures use this simple and quick approach in the preparation of the recipient's cornea. The introduction of the method of stripping the damaged DM and endothelium from the inner surface of the recipient's cornea, without disturbing the deep stromal lamellas, meant a considerable simplification and acceleration of the surgical technique of posterior lamellar keratoplasty. Nevertheless, on the other hand this simplification also presented certain potential disadvantages. In comparison with the previous techniques, in the case of the DSEK method the surface of the donor's lamella is attached relatively roughly to the smooth surface of the posterior surface of the recipient's cornea. In an experimental study on cadaverous bulbs, Terry demonstrated a greater tendency towards postoperative dislocation of the lamella in comparison with the older DLEK technique, and recommended disturbance of the deep stromal lamellas in the periphery of the recipient's cornea (55). Another difference in comparison with DLEK is that this method always adds a certain quantity of stroma. This is caused by the fact that the thickness of the implanted lamella, formed by deep layers of the stroma, DM and endothelium, is always greater than the thickness of the removed lamella, formed only by the DM and endothelium. Nevertheless, Ahmed and Shinton demonstrated in their studies that thickness of the lamella has no influence on the patient's resulting visual acuity (2, 48). Preparation of the donor's lamella and the method of its implantation remained similar as in the previous older DLEK method. Despite the fact that DSEK has in large part been replaced by more modern types of endothelial keratoplasty (DSAEK, DMEK) and the number of published studies on this theme has dropped in recent years, this technique continues to have its justification, primarily at centres where it is not possible to create a donor lamella with the help of a microkeratome, or to obtain such a prepared lamella from a corneal bank.

A further simplification of the surgical procedure took place thanks to the option of preparing the donor lamella with the help of a microkeratome (fig. 5). This procedure was described in the literature in 2006 by Gorovoy (19), who named the operation Descement Stripping Automated Endothelial Keratoplasty (DSAEK). The main advantage of the DSAEK technique is that in comparison with the previous type of operation, preparation of the lamella is relatively easy and fast, as is implantation. The transplanted lamella, similarly as in the case of the previous methods composed of the deep layers of the stroma, DM and endothelium, is created with the help of a microkeratome, or if applicable a femtosecond laser. Above all, for the surgeon the possibility of obtaining tissue prepared in the manner from a tissue bank represents a substantial reduction of the risk of damage to the donor cornea upon preparation of the lamella, and practically eliminates the probability of deferral of the operation for these reasons. A further advantage in comparison with lamellas created manually is the relatively regular thickness of the lamella and relatively smooth surface. For these reasons the method quickly become the most widespread type of endothelial transplant, and probably remains so to this day.

A certain modification of the DSAEK technique is procedures known in the literature as ultrathinDSAEK. The thickness of the lamella in these cases is less than 100 µm. In the case of these very thin lamellas, the published results of visual acuity are

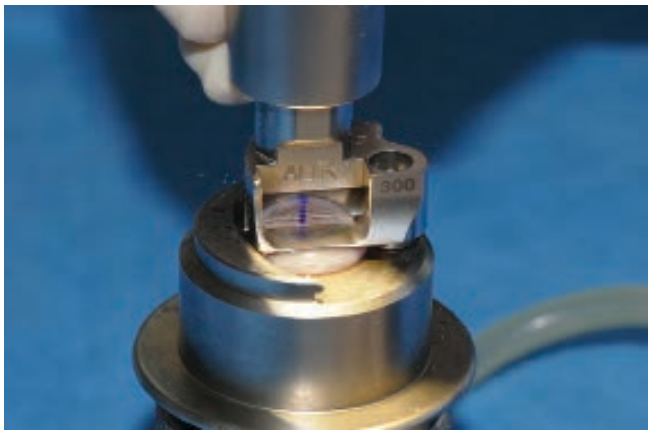

Fig. 5 DSAEK lamella created using a microkeratome

practically comparable with the results of patients following DMEK, whilst retaining all the advantages of DSEAK (10). In order to attain a thinner lamella the technique of dehydration of the stroma is recommended, for example through the use of special solutions or flowing air (57), thus bringing about a reduction of corneal thickness, and the resulting lamella is then thinner upon the use of the same type of microkeratome in comparison with a classic procedure. A further procedure for attaining a very thin lamella is the performance of an incision twice consecutively – the double pass technique (27), which however may lead to greater frequency of damage to the prepared lamella (49). Another option is the use of a femtosecond laser, in which it is possible to individually select the layer in which the incision is to be made (28, 43), although certain authors note worse results in comparison with lamellas created with the help of a microkeratome (24). A possible causes is the greater irregularity on the posterior surface of the patient's cornea following the transplantation of a lamella created by a femtosecond laser (61).

In 2006 Melles described a type of endothelial keratoplasty in which the donor lamella is composed only of the DM and endothelium – DMEK (Descemet Membrane Endothelial Keratoplasty) (34, 45). The tissue is prepared by peeling of the DM from the stroma of the donor's cornea. The main advantage in the case of a successfully performed operation is entirely excellent visual acuity, comparable with vision in the healthy eye. The reason is minimal signs of scarring on the contact surface between the lamellas, since both surfaces (cornea of recipient and lamella of donor) are ideally smooth (21, 23, 43). A disadvantage of the operation is the difficult preparation of the lamella, leading to a relatively high loss rate of corneas and difficult handling of the lamella, including implantation, leading to lower values of postoperative ECD (22, 41). A number of techniques are currently used for preparation of the lamella. The basic technique is the aforementioned manual peeling, in which the DM is removed from the stroma with smooth forceps (31). Giebel and Price described the SCUBA technique, in which the cornea is submerged in optisol or BBS during the course of the preparation, thus reducing surface tension and easing preparation (44). A further technique which eases the separation of the DM from the stroma is pneumatic dissection, in which as a rule a very thin layer of the deep stromal lamellas remains, sometimes referred to as the Dua's layer. We therefore deal with this technique in further detail in the group of transplantations of hybrid lamellas and PDEK (pre-Descemet's Endothelial Keratoplasty) type transplantations. In 2013 Murain described the technique of preparing the separation of the DM with the help of an injection of BSS into the stroma, following partial (330°) superficial trepanning (40). Ruzza compared the formation of a bubble using liquid (tissue medium) and air, in which in the case of liquid a bubble was formed in 100% of cases, in comparison with 80% in the case of gas. Loss of cells was greater in the case of use of air (8.9 ± 12.38% versus 6.25 ± 9.57%), nevertheless the difference was not statistically significant (46). The created lamella of the DME type, in contrast with other types of lamellas, has a tendency to roll outwards in the direction of the endothelium. The implantation technique may be similar as in the case of the previous types of transplantation, or if applicable, due to the very small volume of tissue, it is possible to use absorption of the rolled tissue into the mouth of a plastic cartridge or pipette and its repeat release in the anterior ocular chamber. In summary, the DMEK method according to published studies represents an excellent solution for affliction of the corneal endothelium, since a large proportion of patients attain visual acuity of 1.0. In addition, certain types of complications such as rejection, damage to the anterior segment of the eye during the course of surgery and refractive changes are described only very rarely. On the other hand detachment of the lamella with the necessity of re-bubbling is stated relatively often, and in certain publications also a higher loss of endothelial cells. In the Czech Republic experiences with this technique have been described by Hlinomazová et al. (25).

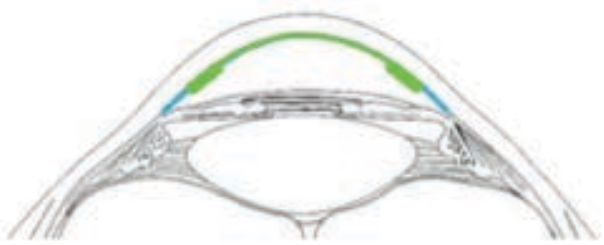

Fig. 6 Schematic illustration of hybrid type of lamella (in green transplanted endothelium, DM, stroma, in blue original endothelium)

In an endeavour to simplify the preparation of a DMEK type lamella and ease handling of tissues during the course of implantation into the eye of the recipient, in 2010 our team described the preparation of the hybrid type of lamella DMEK-S (Descement Stripping Endothelial Keratoplasty with Peripheral Stromal Support), which in the central part is formed by the DM and endothelium, and in the peripheral parts supporting deep layers of the corneal stroma remain (fig. 6) (52, 53). This lining enables handling of the lamella during the course of implantation, as well as unfolding of the lamella in the anterior chamber of the recipient. For peeling of the DM during the preparation of the lamella we used the above-described technique of pneumodissection, using the "big-bubble" phenomenon, in which spontaneous separation takes place following an injection of

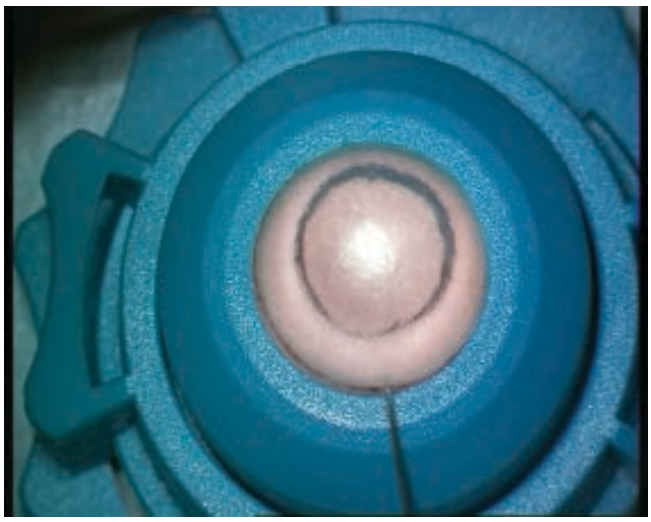

Fig. 7 Pneumodissection (big-bubble)

air into the corneal stroma (fig. 7). The big bubble technique was described previously by Anwar and Teichmann in the case of deep lamellar keratoplasty (8). Our study was followed on from for example by McCauley and Pereira, who create a hybrid lamella from a lamella created by a keratome. They named this modification DMAEK (Descement's Membrane Automated Endothelial Keratoplasty) (32, 42). Busin created a supporting stromal lining in part of the lamella with the help of eccentric trepanning of the lamella. For separation of the stroma from the DM he also used pneumatic dissection (11). Although hybrid types of lamellas theoretically combine the advantages of DMEK and DSAEK operations – excellent postoperative visual acuity and relatively easy handling, in the studies published to date a relatively high frequency of complications has been demonstrated, above all failure of attachment of lamella, greater shrinkage of endothelium and relatively high percentage of primary failure. Despite this fact, this technique may be of significance for example in the case of complicated operations, for example in eyes following pars plana vitrectomies, with rough anatomical changes of the anterior ocular segment or in the case of resolving failure of the endothelium following PKP, in which simple handling and easy unfolding of the lamella in the anterior chamber may be a great advantage (7).

The last type of endothelial keratoplasty to date is PDEK, or pre-Descemet's Endothelial Keratoplasty, in which a lamella is formed by the "Dua's layer", the DM and the endothelium. The preparation of the lamella again takes place using the big bubble technique, similarly as in the case of a hybrid DMEK-S type lamella, nevertheless the lamella does not have a supporting stromal lining in the periphery (1). Although this is the most recently introduced surgical method of transplantation in the literature, in reality it has been used for a longer time. The fact that a fine layer of the stroma is also present in DMEK lamellas created by pneumodissection was first noted by McKee, who demonstrated this fact histologically in an experiment on 5 corneas from a tissue bank. Average thickness of the stroma was 12.4 µm (range 6.5-20.0 µm) (33). There was a subsequent redefinition of the anatomical structure of the cornea, and the Duo layer was newly introduced – a thin collagen layer between the stroma and the DM (13, 15), although other authors doubt the existence of this layer (47). In an experiment on donor corneas, Dua created 3 types of bubble using the big-bubble technique: a classic bubble created in the centre of the cornea, as a rule up to a size of 8.5 mm in diameter, which is created most frequently, also a thin-walled large bubble with a diameter up to 10.5 mm, which always begins in the periphery, and a mixed type of bubble which occurs less frequently. Precisely upon the creation of a classic bubble (type I) a thin collagen layer is present on the lamella. In the case of the thin-walled type (II) the actual DM is exposed (13). In an experiment on 21 donor corneas, Gamaleldin separated the DM in 20 corneas (95%) using the big-bubble technique, in 14 cases a Dua layer was also a component of the lamella (18). This layer contains collagen VI and in a certain manner links to the spaces of iridocorneal angle (spatia anguli iridocornealis). Cells of the spaces of iridocorneal angle (spatia anguli iridocornealis) CD34 were found in its periphery, and collagen VI spreads from the Dua layer into the tissue of the spaces of iridocorneal angle (spatia anguli iridocornealis) (14). On the basis of these facts, for transplantation of the endothelium, in which a lamella obtained by the technique of pneumodissection is used, Agarwal introduced the more accurate term pre-Descemet's Endothelial Keratoplasty (PDEK).

CONCLUSION

In pathologies primarily afflicting the corneal endothelium, today one of the techniques of posterior lamellar keratoplasty is the method of choice. According to the number of published studies, probably the most popular technique at present is the technique using the DSAEK method, above all due to its relative simplicity. Nevertheless, the best results are demonstrated by patients following DMEK or PDEK type operations, which with regard to the minimal inter-lamellar scarring, small influence on the refractive state of the eye and quick convalescence enable us to attain practically optimal visual acuity very quickly. Nevertheless, the relatively substantial technical demand factor, both in the preparation of the lamella and in the actual implantation, have so far meant that this method has not become widespread. Further observation shall be required, as well as the development of techniques in the preparation of the lamella and its subsequent implantation. Further possibilities in future could be for example the cultivation of endothelial cells in vitro and their transplantation on a support, or induction of the conditions for the theoretical possibility of reproduction and renewal of the patient's own endothelial cells.

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