Morphological Screening of Donor Corneal Tissue for Previous Refractive Surgery

Chinh Nguyen, MBBS[1]; Chameen Samarawickrama, MBBS, PhD[2,3]
Rasik Vajpayee, FRANZCO[2]

ABSTRACT

Purpose: A major concern for eye banks internationally is the detection on routine screening of corneas with previous corneal refractive surgery. It is increasingly becoming a concern with the rise in prevalence of refractive surgery in our community and the variety of refractive procedures available. Inadvertent transplantation of corneas with previous refractive surgery can have serious visually significant sequelae varying from unexpected refractive surprises to tectonic compromise. Morphological screening has undergone significant changes as recovery of corneoscleral rims for corneal donation has increased in frequency to the older technique of whole globe enucleation. The current screening protocols, namely using slit lamp biomicroscopy of tissue stored in transport media coupled with a medical history, has been shown to be fallible. To overcome this shortfall, new technology such as specular microscopy, corneal topography and optical coherence tomography have been employed to improve the detection rate of previous corneal refractive surgery. However, there are major limitations that have prevented their widespread use. The newer screening modalities are better suited to screening whole globes rather than corneoscleral rims and for effective utilization the technology has to be compatible with both tissue recovery techniques. No single modality has been shown to be adequate in detecting the full variety of refractive procedures. In addition the technology has to be cost effective for eye banks to incorporate them into their screening protocols. This review summarizes the literature to date on screening techniques currently available and their utility in detecting previous refractive surgery in donor corneas.

Keywords: refractive surgery, eye banking, corneal tissue, screening, whole globe enucleation, corneoscleral rim

The rise in refractive surgery in recent years raises concerns about the quality of donor corneas within eye banking systems.(1) While the Eye Bank Association of America (EBAA) specifies that previous refractive surgery is an absolute contraindication for anterior corneal transplants, it has yet to adopt a screening method that guarantees corneas have not had previous refractive surgery.[1] This corresponds to the increasing number of reported cases of erroneous transplantation of corneas with previous refractive corrections.[2-4] This is not so much an issue with endothelial keratoplasty, where previous refractive surgery in donor corneas does not affect quality of corneal endothelium.[5] The risks involved include postoperative ametropia and irregular astigmatism from unmatched refractive corrections and displaced optical zones as well as reduced structural integrity from transplanting tissue of reduced thickness and previous laser in-situ keratomileusis (LASIK) flaps.[6]

This issue has long been recognised by the ophthalmology community, and subsequently, several screening methods have been suggested to identify corneas with previous keratorefractive surgery. Much of the technology developed is based on measurements of corneal curvature, thickness and structural changes, which currently are better suited to screening whole globes rather than corneoscleral rims. In selecting the most appropriate method for wide-spread use in eye banks, sensitivity/specificity, availability and cost-effectiveness are some of the factors to be considered.[7] This review evaluates and compares these alternate screening methods, and attempts to draw conclusions on the most appropriate screening technique.

CURRENT EYEBANK METHOD

Recovery, Processing and Tissue Evaluation

Tissue recovery can be performed via enucleation or in-situ corneoscleral rim collection.[1] Povidone-iodine solution is applied to reduce bioburden. Prior to harvesting, the cornea is examined by the technician with a penlight or porta-

Author Affiliations: [1]Royal Melbourne Hospital, [2]Royal Victorian Eye and Ear Hospital, [3]Sydney University

Corresponding Author: Chameen Samarawickrama, Royal Victorian Eye and Ear Hospital, 32 Gisbourne St, East Melbourne, 3002, VIC phone: +61 3 9929 8666, email: chameensams@gmail.com

Author Disclosures: No conflict of interest for any author

ble slit lamp for surface defects including clarity, epithelial defects, foreign objects, contamination and scleral colour[1] and the detection of defects is dependent on the quality of their training. Whole globes intended for transplant are preserved in a moist chamber at 2-8°C, freezing below 0°C or some other validated method. While corneoscleral rims are processed via excision of the corneoscleral disc from enucleated whole eyes or via microkeratome/femtosecond laser for lamellar tissue processing and stored in culture medium at 4°C for short term preservation.[1] There is increasing use of long-term preservation and organ culturing in Europe, allowing globes to be procured up to 72 hours postmortem and corneoscleral discs to be stored in organ culture and then transplanted with good corneal outcomes.[1] Depending on the intended use of the corneal tissue, slit lamp biomicroscopy, endothelial cell density and pachymetry measurements are undertaken.[1] In combination with these microscopy techniques, history of previous intraocular or refractive surgery is also elicited from medical records or family members of the donor.[1]

Whole Globe Enucleation Versus In Situ Corneoscleral Rim Excision

Many eye banks are moving towards in situ excision of corneoscleral rims as it is simpler and less invasive and disfiguring to donors.[8] Further, corneoscleral rim collection has the added benefit of reducing the death-to-preservation time, as donor corneas are immediately placed into culture medium post extraction.[9] The feasibility of such a method is comparable to the whole globe enucleation in terms of contamination risk, endothelial cell count and quality of the recovered tissue (Table 1). [10,9,11, 12,11-13]

Limitations to the Current Screening Method

Slit lamp biomicroscopy has low sensitivity and specificity for detecting LASIK flaps and limited ability in identifying superficial refractive procedures (photorefractive keratectomy (PRK) or laser assisted sub-epithelium keratomileusis).[14, 15] Mootha et al showed a 15% false negative rate in slit lamp biomicroscopy failing to detect LASIK flaps,[14] while Kang et al demonstrated a 18.5% false positive rate in misidentifying normal corneas as having had previous LASIK.[15] Further, once the corneoscleral disc has been harvested, corneal topography cannot be performed. While consulting medical records and taking history from family members may help to increase the detection rate, a more reliable screening technique is needed to identify corneas that have had previous refractive procedures.

ALTERNATE PROPOSED SCREENING METHODS

Many methods attempt to identify the characteristic changes in corneal macro and micro structures to distinguish normal corneas from those that have had previous refrac-

Paper	Number of cases	Conclusions
Schroeter et al (2012)(9)	975 enucleation eyes 1830 in situ excision of corneoscleral rims	Rate of microbial contamination in organ-cultured donor corneas does not depend on the method of their retrieval.
Kim et al (2010)(11)	3618 enucleation eyes 2048 in situ excision of corneoscleral rims	Endothelial cell density, level of acceptability for transplantation and post-operative infection levels were comparable between the two groups.
Jhanji et al (2008)(12)	50 enucleation eyes 50 in situ excision of corneoscleral rims	No statistical differences in endothelial cell count, contamination rate or graft clarity between the two groups.
Rootman et al (2007)(13)	168 enucleation eyes 300 in situ excision of corneoscleral rims	In situ procurement of corneal tissue results in higher initial corneal tissue quality than whole-globe procedures
Lane et al (1994)(10)	24 enucleation eyes 24 in situ excision of corneoscleral rims	Less tissue contamination and endothelial cell trauma with standard enucleation compared to in situ excision of corneoscleral rims.

Table 1*: current literature available comparing whole eye to rims*

tive surgery. Corneal topography, pachymetry and internal stromal flap reflectivity are some of the key measurements suggested. The instruments employed range from slit lamp examination and specular microscopy, which are available in most eye banks, to the more advanced systems, including computerized videokeratography, corneal topography and optical coherence tomography (OCT). Amongst these instruments, various algorithms have been tested to allow for a more objective, consistent and encompassing screening method (Table 2).

Recoverytechnique	Screening methods available
Whole Globe	Slit Lamp Biomicroscopy Videokeratography Orbscan Optical Coherence Topography
Corneoscleral rim	Light microscopy Specular Microscopy Confocal microscopy Optical Coherence Topography
Both whole globe & corneoscleral rim	Optical Coherence Topography

***Table 2**: screening techniques available by harvest technique*

Slit Lamp Biomicroscopy — Screening of Whole Globes for PRK

The current slit lamp method does not allow for the detection of refractive surgery without corneal flaps, such as PRK.[14] However, Kanavi et al showed that by altering the method of tissue preparation, slit lamp biomicroscopy can be improved to enable the detection of such donor corneas.[16] Donor globes are first immersed in povidone-iodine solution for 3 minutes, prior to slit lamp examination and corneas exhibiting a disciform, hazy area within the central 8mm of the cornea, representing the sloughing of the loosely attached epithelium overlying the PRK treated area, is suggestive of previous PRK. In their study, twenty corneas with suspected PRK were evaluated against 57 controls using this method and all 20 were detected and confirmed with histopathology to have undergone PRK.[16]

Other advantages of this method include its cost-effectiveness, accessibility and efficiency. However, it is limited to the whole globe technique of donor cornea recovery and only for the detection of previous PRK.

Specular Microscopy for Detection of LASIK Interface

Specular microscopy is currently being used to evaluate the endothelial cell count density of donor corneas and may prove beneficial in detecting a LASIK flap. Previously, in vivo confocal microscopy revealed the presence of highly reflective particles in the corneal interface post LASIK,[17-19] which is thought to be vacuolisation and pyknosis of keratocytes along the lamellar cut.[14] Specular microscope is a reflected light microscope similar to confocal microscopy and is able to detect the presence of highly reflective particles in the LASIK flap interface.[14] A prospective study by Mootha et al evaluated 26 donor LASIK corneas against 26 control normal corneas and showed that specular microscopy was able to identify highly reflective particles in 23 of 26 (88%) cases of LASIK performed as far back as 4.5 years and as early as 9 days.[14]

Given the wide availability of specular microscopes this method is inexpensive, though time consuming, and can be readily implemented. However, it is only appropriate for screening corneas with stromal flaps. Further, the study failed to establish the sensitivity and specificity of the method, and is an area that needs further research.[14]

Computerized Videokeratography to Screen PRKs Using Corneal Topography

Changes to corneal topography are expected in corneas with previous keratorefractive surgery. Thus, characterisation of changes in corneal curvature may be useful as a screening tool. Various instruments have been developed to evaluate corneal topography including the placido disk computerized videokeratography.

Lim-Bon-Siong et al, evaluated the effectiveness of computerized videokeratography as a screening tool for detecting myopic PRK.[20] 12 normal human donor corneas were given myopic PRKs in the laboratory and preoperative and postoperative topographic maps were compared. Similarly, 12 rabbit eyes received refractive treatment with harvesting and analysis performed 6 weeks post PRK. Both groups demonstrated the characteristic bull's-eye pattern with central corneal flattening, with the study concluding that this topographic technique reliably detects all laser-treated eyes of both human and rabbit models.[20]

Further, two methods of evaluating corneal curvatures were compared, the newly developed tangential mapping against the existing axial-formula based colour maps. In a preliminary study, three patients who had myopic PRK ablations of -1.5 to -3D at least 6 months previously were compared. Despite the absence of myopic regression on refraction, colour map topography was unable to detect the previous PRK while tangential mapping clearly demonstrated the bull's eye pattern.[20] Larger studies are needed to convincingly demonstrate the superiority of the newer imaging algorithm as well as to determine if computerized videokeratography has a role in detecting corneas with refractive surgery apart from PRK.

Computerized videokeratograph is an expensive technology and can only be used on whole globes, as artificial elevation of intraocular pressure is required.[20] This is a significant limitation as in situ excision of the corneoscleral rim is the preferred method in nearly half of the retrievals worldwide. Further, contact is required when measurements are made, potentially increasing the risk of microbial contamination.[20]

Portable Topography for Screening at Donor Sites

The Keratron Scout portable topographer, an advancement on table top topography systems, was designed to evaluate corneas at donor sites prior to enucleation or in situ excision of corneoscleral rims.[21] This helps screen for defective corneas, avoiding unnecessary removal of tissue.

Ousley and Terry evaluated corneal topography obtained with the Keratron Scout before (at donor sites) and after whole-eye enucleation (in the laboratory.[21] 22 eyes of 12 normal donors were studied; field and laboratory measurements of central curvature, astigmatism, and the difference between the corneal curvature at the 7mm and 3mm zone were compared. The 7mm and 3mm zone curvature differences were measured to establish the normal range, which may be used to screen corneas with prior refractive surgeries. The central curvature and astigmatism between field and laboratory measurements were comparable, as were the curvature differences between the 7mm and the 3mm zone in the field and laboratory.[21] All eight corneas with myopic refractive surgeries and one of two eyes with hexagonal keratotomy for hyperopia were flagged as lying outside 2 standard deviations of the normal range of the curvature difference at 7mm and 3mm zone.[21] These results suggest the Keratron Scout can be employed for measurements both at donor sites and in the eye bank laboratory with comparable results. Once again, however, further studies are needed to validate these results and determine its usefulness in detecting the variety of refractive surgery available.

This portable system may circumvent the problem of topography not being able to be used on corneoscleral rims, as measurements can be made prior to tissue collection. The Keratron Scout is substantially cheaper than similar desktop topography units, and it can be mounted onto a table top for laboratory evaluations if needed.[21] Given its diverse use, relative low cost, unique portability and the ability to make measurements before in situ excisions, the Keratron Scout may be a promising screening tool for wide spread use. However, contact with the cornea is still required with this instrument.

Combined Corneal Topography and Pachymetry Measurements

Aside from topography, corneal thickness can also be measured for screening. Terry and Ousley first demonstrated that the average difference between the thinnest midperipheral pachymetry and central corneal pachymetry can be used to screen for refractive surgery in donor corneas.[21] A later study with higher numbers of donor corneas that had undergone various refractive surgeries (refractive keratectomy, PRK and LASIK) combined with corneal topography (Orbscan) the detection rate increased to 7 of 10 (70%) eyes.[22]

Laliberte et al further developed this combined technique using new automated measurement algorithms in the analysis of corneas with previous LASIK.[23] The first algorithm calculated the volume summation between the best-fit sphere in the central and mid-peripheral regions while the second set of algorithm examined the mean anterior tangential curvature difference between the central and mid-peripheral regions. Both techniques demonstrated similar sensitivity and specificity of above 92%.[23] Hick et al went on to add another criteria for screening by evaluating the difference between anterior and posterior central corneal elevations, which yielded a similar sensitivity and specificity of 90% and 92.5%, respectively.[24]

The combined pachymetry and corneal topography algorithm based methods allow objective evaluation that is consistent and not operator dependent. However, similar to videokeratography, it can only be used on whole globes and requires contact with the corneal surface for measurement, posing a risk for microbial infections.

Optical Coherence Tomography

Optical coherence tomography (OCT) is a non-invasive, noncontact method for acquiring optical cross-sections of the eye and is effective in screening donor corneas for structural changes. Unique to its function, OCT can perform corneal pachymetry, topography and reflectivity measurements through the storage media, without the need for contact of the corneal surface.[25, 26] Importantly, measurements can be made on both whole globes and corneoscleral rims, allowing its use in both harvesting techniques.[25]

High-resolution OCT has been shown to accurately detect LASIK flap interfaces in donor corneas through direct visualisation.[27] Priglinger et al demonstrated in normal human donor corneas that underwent LASIK in the laboratory and were analysed at various flap depths and at different intervals post-surgery (up to 6 months) that OCT was able to identify the flap interface in all studied corneas and at all examined time intervals.[27] The signal decreased over time during the 6 month observation period in 20% of the organ-cultured corneas; nonetheless, they remained detectable with OCT.[27] A case study reported OCT detection of LASIK flaps up to 9 months post-operation.[28]

More recently, Verrier et al devised an objective OCT evaluation of LASIK flaps using an in vivo and in vitro animal model of rabbit eyes.[6] LASIK was performed on normal rabbit eyes after whole globe enucleation in one group and in live rabbits in the second group, with analysis made at 1month post refractive surgery. This enabled low flap signals, otherwise undetectable, to be amplified and display on the monitor as the second peak.[6] Further study is required for analysis on human eyes.

With time LASIK flaps become more integrated with the stroma, and by the 3rd year post-surgery, the interface can no longer be directly visualised by OCT and the internal LASIK flap reflectivity become lower than that of the posterior stroma.[25] A study by Lin et al[25] analysed 5 donor LASIK corneas, where flaps could not be visualised under slit lamp or OCT. However, it was noted that the anterior/posterior stromal reflectivity ratios in corneas with LASIK were consistently lower than that of control corneas, especially in the central 2mm diameter and in the annular region from 2 to 4mm in diameter.[25] Further, using OCT topography, the authors were able to demonstrate statistically significant differences in the central anterior curvature between the LASIK group and non-LASIK group, with the LASIK corneas exhibiting a flatter anterior surface, as expected in myopic keratorefractive surgery.[25] The same principle could be applied to screen corneas with other types of refractive surgeries.

DISCUSSION

While an array of instruments have been trialled to screen for donor corneas with refractive surgery, this review demonstrates a clear lack of robust large clinical studies evaluating the sensitivity and specificity of these screening methods, as well as their accessibility and cost effectiveness. Most of the trials mentioned failed to recruit adequate study participants to arrive at meaningful conclusions, with many not employing the use of controls to establish a specificity value to determine the accuracy of the instruments. Furthermore, many of the studies were not blinded. As the majority of these screening techniques were tested only on donor corneas with one type of refractive surgery, extrapolation of these data to other forms refractive surgeries cannot be made. This brings into question the widespread application of these instruments. These studies are summarised in Table 3.

Examining the available data indicates that the Orbscan II algorithm based topography is the most effective and accurate instrument to screen for donor corneas. The study by Laliberte et al employed a large n number (n = 476), resulting in a high sensitivity (93-95%) and specificity (95-97%).[23] The algorithm-based methods were further validated against four experienced LASIK surgeons, whose manual interpretations of Orbscan topographies yielded a lower sensitivity (84%), with a similar specificity (96%).[23] Nonetheless, the study was limited to LASIK corneas and thus, cannot be applied to other forms of refractive surgeries.[23] In addition, Orbscan measurements require contact with the corneal surface.

With its varied applications and non-contact technique, OCT has the potential to be the instrument for widespread use. However, further studies are needed to validate its application, with larger n numbers.

CONCLUSIONS

The rapid rise in refractive surgeries is a major concern for eye banks, with increased reported incidence of transplantation of corneas with prior keratorefractive surgery. Slit lamp biomicroscopy has low accuracy for detection of LASIK flaps and is unable to screen for refractive surgeries without corneal flaps. In considering the most appropriate screening method for widespread use in eye banks, cost-effectiveness, ease of use and high level of accuracy for a wide range of refractive surgery are some of the factors to be considered (Table 3).[7]

Further studies are needed to expand the literature currently available in each screening technique. From the current literature, slit lamp biomicroscopy in combination with povidone-iodine and specular microscopy looking for high reflective particles are potential tools to screen for PRK and LASIK, given their widespread availability in eye banks.[14, 16] The limitations of topographic instruments mainly concern their inability to be utilised when recovering corneoscleral rims (ameliorated in the portable models). OCT can evaluate corneas through a diverse range of measurements, including direct visualisation, topography, pachymetry and LASIK flap reflectivity.[25, 27] It can be used on both whole globes and corneoscleral rims, without the need to remove the tissues from the storage media.[26] Nonetheless, in order for OCT to be considered for widespread use, further studies are required to validate the instrument and to assess its cost-effectiveness.

Method	Application	Method	Type of study	Detection rate	Time from surgery	Comment on the study
Slit lamp(16)	Whole globe PRK Myopia	Povidone iodine treatment of donor corneas. Examination under slit lamp for central hazy disciform area.	Blinded Prospective 20 donors 57 controls	(20/20) 100% sens (57/57) 100% spec	n/a	Level of evidence – Moderate (small n number). High sensitivity and specificity. Limited to PRK. Nil indication of time from refractive surgery.
Specular microscopy(14)	Whole globe LASIK Myopia	Examination of LASIK donor corneas under specular microscopy, looking for maximal number of highly reflective particles at flap edge.	Non-blinded Prospective 26 donors 26 controls	88% sens 96% spec	9d– 4.5y	Level of evidence – Low. Operator dependent. Time consuming. No quantitative definition of a highly reflective particle. Limited to LASIKs.
Computerized Videokeratography (20)	Whole globe PRK Myopia	Normal human donor eyes and rabbit underwent PRK. Topographic examination looking for bull's eye pattern.	Non-blinded Prospective 12 humans 12 rabbits	100% sens n/a - spec	Humans (n/a) Rabbits (6w)	Level of evidence – Low (small n numbers & no specificity). Nil indication of time from refractive surgery for human corneas. The alternative tangential method of measurement required further validation (n = 4)
Portable topography(21)	Whole globe at donor site. RK, LASIK, HK	Comparison between portable keratron topographer's accuracy at donor site and at the laboratory. Differences between regional corneal curvature at 7mm and 3mm zones were evaluated to establish a "normal" range (mean +/- 2 SD). Donor corneas' regional differences in curvature were then compared to the established "normal range" (outside normal range of mean +/- 2 SD).	Non-blinded Prospective 9 donors 22 controls	100% sens n/a - spec	2m-13y	Level of evidence – Low (small n number & no specificity). Nonetheless, comparable results when used at donor site and at the laboratory.
Orbscan – Topography and pachymetry(21, 22)	Whole globe RK(n=2), PRK (n=2), LASIK (n=6)	*Pachymetry method*: Compare the regional thickness difference between the thinnest mid-peripheral and central cornea. Controls were used to establish the "normal" range (mean +/- 2 SD). *Topography method*: Compare the regional corneal curvature difference between the 7mm and 3mm zones. Controls were used to establish the "normal" range (mean +/- 2 SD).	Non-blinded Prospective 10 donors 22 controls	*Pachymetry*: (3/10) 30% sens (1/22) 95% spec *Topography*: (4/10) 40% sens (3/22) 86% spec *Combined*: (7/10) 70% sens (4/22) 82% spec	6.5m – 6y	Level of evidence – Low (small n numbers). Low sensitivity and specificity.
Orbscan – Algorithm based topography(23)	Whole globe LASIK for myopia(n=81) LASIK for hyperopia(n=5)	Algorithm 1: Volume summation between the anterior corneal surface and the best-fit sphere in the central and mid-peripheral regions. Algorithm 2: Calculated the mean anterior tangential curvature difference between the central and mid-peripheral regions. Performances of 4 experienced clinicians were then compared to that of the algorithms.	Blinded Prospective Myopia total n=239 Hyperopia total n=237 Myopia/LASIK (n=81) Hyperopia LASIK for (n=57)	*Algorithm 1*: 93% sens 95% spec *Algorithm 2*: 95% sens 97% spec *Clinicians*: 84% sens 96% spec	Mean 4.4m	**Level of evidence – High (large n number).** High sensitivity and specificity. High correlations between algorithm 1 and 2. Higher detection rate compared to experienced clinicians. Limited to LASIKs.
OCT – Direct visualisation(27)	Whole globe LASIK	LASIKs performed on normal donor corneas, with ablation ranging from 0-12 diopters. Direct visualisation of LASIK flaps up to 6 months post LASIK surgery.	Non-blinded Prospective 20 donors 0 controls	100%sens n/a spec	1m-6m	Level of evidence – Low (small n number & no specificity). High detection rate (sensitivity). Assessment of wide range of diopters. Limited to LASIKs.
OCT – Reflectivity ratio & anterior curvature(25)	Whole globe LASIK	Method 1: Measurement of anterior/posterior reflectivity ratio in the central 4mm diameter. Method 2: Measuring anterior corneal curvature.	Non-blinded Prospective 5 donors 24 controls	100% sens 100% spec	3-4y	Level of evidence – Low (small n number). Limited to LASIK.

***Table 3**: summary of screening techniques with methods and results.*

METHODS OF LITERATURE SEARCH

A search of the MEDLINE and Cochrane Library databases were conducted (CN) during October 2014 using the following key words: Eye Bank Association of America, eye bank recovery method, whole globe enucleation, corneoscleral rim, in-situ excision, corneal contamination, corneal screening methods, corneal screening: slit lamp, specular microscopy, videokeratography, orbscan, optical coherence topography. The search covered all published literature until September 2014. The review was limited to peer-refereed papers published in English including all age groups. Bibliographies of identified studies were hand searched for further references. Search results were collected and abstracts screened to remove any articles clearly not relevant to the topic. Total references for the review is 27. The manuscript was edited by CS and RV.

REFERENCES

1 Eye Bank Association of America. Medical Standards. Washington, DC: Eye Bank Association of America. 2013 November.

2 Michaeli-Cohen A, Lambert AC, Coloma F, Rootman DS. Two cases of a penetrating keratoplasty with tissue from a donor who had undergone LASIK surgery. Cornea. 2002 Jan;21(1):111-3.

3 Mendez Angulo E. Accidental grafting of a donor cornea with radial keratotomy in a keratoconus patient. *Refractive & corneal surgery.* 1989 May-Jun;5(3):198.

4 Maharana P, Jhanji V, Vajpayee RB. Inadvertent use of cornea with previous LASIK in deep lamellar keratoplasty. *Optometry and vision science* : official publication of the American Academy of Optometry. 2014 Mar;91(3):e59-62.

5 Ple-Plakon PA, Shtein RM. Trends in corneal transplantation: indications and techniques. *Current opinion in ophthalmology*. 2014 Jul;25(4):300-5.

6 Verrier I, Veillas C, Lepine T, Nguyen F, Thuret G, Gain P. Interfaces detection after corneal refractive surgery by low coherence optical interferometry. *Biomedical optics express.* 2010;1(5):1460-71.

7 The Lewin Group, Inc. Cost-Benefit Analysis of Corneal Transplant — Prepared For Eye Bank Association of America. Virginia 2013 9 september 2013.

8 Jones GL, Ponzin D, Pels E, Maas H, Tullo AB, Claerhout I. European eye bank association. *Developments in ophthalmology.* 2009;43:15-21.

9 Schroeter J, Wilkemeyer I, Herrlinger F, Pruss A. Comparison of in situ Corneoscleral Disc Excision versus Whole Globe Enucleation in Cornea Donors Regarding Microbial Contamination in Organ Culture Medium — a Prospective Monocentric Study over 9 Years. Transfusion medicine and hemotherapy: offizielles Organ der Deutschen Gesellschaft fur Transfusionsmedizin und Immunhamatologie. 2012 Dec;39(6):391-4.

10 Lane SS, Mizener MW, Dubbel PA, et al. Whole globe enucleation versus in situ corneal excision: a study of tissue trauma and contamination. *Cornea*. 1994 Jul;13(4):305-9.

11 Kim JH, Kim MJ, Stoeger C, Clover J, Kim JY, Tchah H. Comparison of in situ excision and whole-globe recovery of corneal tissue in a large, single eye bank series. *American journal of ophthalmology*. 2010 Sep;150(3):427-33 e1.

12 Jhanji V, Tandon R, Sharma N, Titiyal JS, Satpathy G, Vajpayee RB. Whole globe enucleation versus in situ excision for donor corneal retrieval--a prospective comparative study. *Cornea*. 2008 Dec;27(10):1103-8.

13 Rootman DB, Wankiewicz E, Sharpen L, Baxter SA. In situ versus whole-globe harvesting of corneal tissue from remote donor sites: effects on initial tissue quality. *Cornea*. 2007 Apr;26(3):270-3.

14 Mootha VV, Dawson D, Kumar A, Gleiser J, Qualls C, Albert DM. Slitlamp, specular, and light microscopic findings of human donor corneas after laser-assisted in situ keratomileusis. *Archives of ophthalmology*. 2004 May;122(5):686-92.

15 Kang SJ, Schmack I, Edelhauser HF, Grossniklaus HE. Donor corneas misidentified with prior laser in situ keratomileusis. *Cornea*. 2010 Jun;29(6):670-3.

16 Kanavi MR, Javadi MA, Chamani T, Javadi A. Screening of donated whole globes for photorefractive keratectomy. *Cornea*. 2011 Nov;30(11):1260-3.

17 Pisella PJ, Auzerie O, Bokobza Y, Debbasch C, Baudouin C. Evaluation of corneal stromal changes in vivo after laser in situ keratomileusis with confocal microscopy. *Ophthalmology*. 2001 Oct;108(10):1744-50.

18 Gokmen F, Jester JV, Petroll WM, McCulley JP, Cavanagh HD. In vivo confocal microscopy through-focusing to measure corneal flap thickness after laser in situ keratomileusis. Journal of cataract and refractive surgery. 2002 Jun;28(6):962-70.

19 Sonigo B, Chong Sit D, Ancel JM, Auclin F, Bokobza Y, Baudouin C. [In vivo confocal microscopy evaluation of corneal changes induced after LASIK using the IntraLase femtosecond laser technique]. *Journal francais d'ophtalmologie*. 2005 May;28(5):463-72.

20 Lim-Bon-Siong R, Williams JM, Samapunphong S, Chuck RS, Pepose JS. Screening of myopic photorefractive keratectomy in eye bank eyes by computerized videokeratography. *Archives of ophthalmology*. 1998 May;116(5):617-23.

21 Ousley PJ, Terry MA. Use of a portable topography machine for screening donor tissue for prior refractive surgery. *Cornea*. 2002 Nov;21(8):745-50.

22 Ousley PJ, Terry MA. Objective screening methods for prior refractive surgery in donor tissue. *Cornea*. 2002 Mar;21(2):181-8.

23 Laliberte JF, Meunier J, Hick S, Brunette I, Canadian Refractive Surgery Research G. Topography-based screening for previous laser in situ keratomileusis to correct myopia and hyperopia. *Cornea*. 2005 Mar;24(2):167-77.

24 Hick S, Laliberte JF, Meunier J, Ousley PJ, Terry MA, Brunette I. Topographic screening of donor eyes for previous refractive surgery. *Journal of cataract and refractive surgery*. 2006 Feb;32(2):309-17.

25 Lin RC, Li Y, Tang M, et al. Screening for previous refractive surgery in eye bank corneas by using optical coherence tomography. *Cornea*. 2007 Jun;26(5):594-9.

26 Neubauer AS, Priglinger SG, Thiel MJ, May CA, Welge-Lussen UC. Sterile structural imaging of donor cornea by optical coherence tomography. *Cornea*. 2002 Jul;21(5):490-4.

27 Priglinger SG, Neubauer AS, May CA, et al. Optical coherence tomography for the detection of laser in situ keratomileusis in donor corneas. *Cornea*. 2003 Jan;22(1):46-50.

28 Ustundag C, Bahcecioglu H, Ozdamar A, Aras C, Yildirim R, Ozkan S. Optical coherence tomography for evaluation of anatomical changes in the cornea after laser in situ keratomileusis. *Journal of cataract and refractive surgery*. 2000 Oct;26(10):1458-62.

