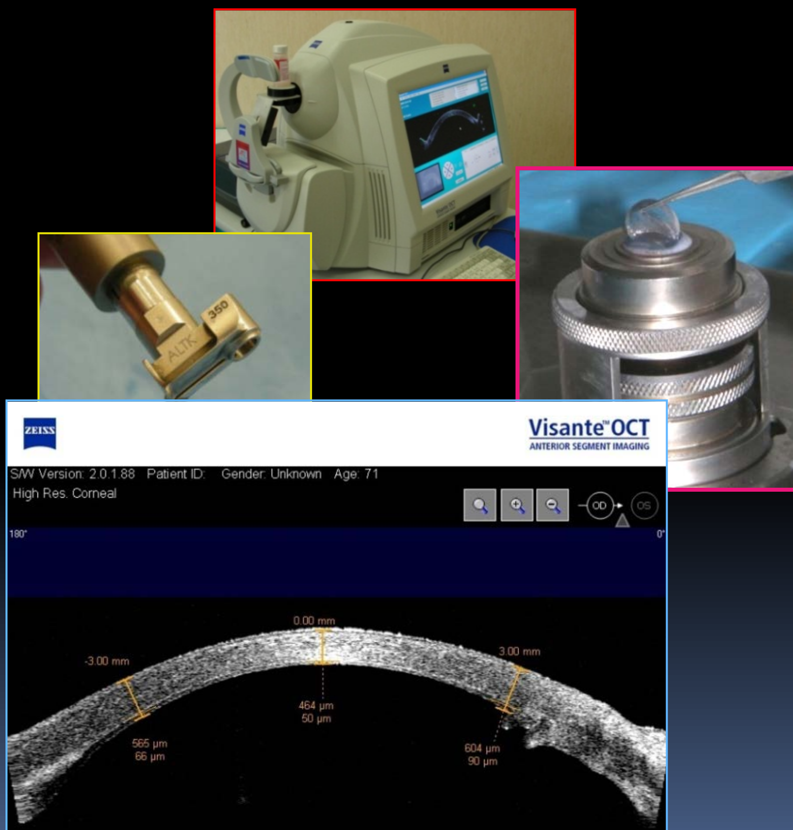
CHERATOPLASTICHE LAMELLARI ENDOTELIALI : STANDARD vs FSL



Augusto Pocobelli

Azienda Ospedaliera
S. Giovanni Addolorata
Roma - Italy

L'Aquila 24 novembre 2012

Endothelial keratoplasty: DSEK/DSAEK or DMEK - the thinner the better?

Isabel Dapena[a,b], Lisanne Ham[a,c] and Gerrit R.J. Melles[a,b,c]

Current Opinion in Ophthalmology 2009, 20:299–307

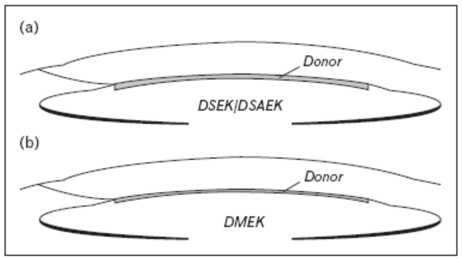
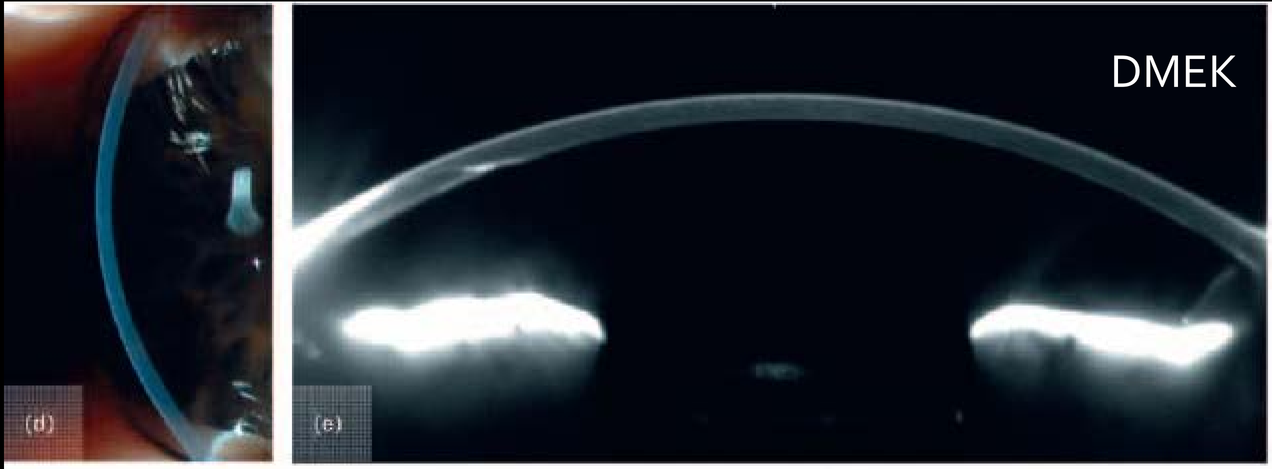
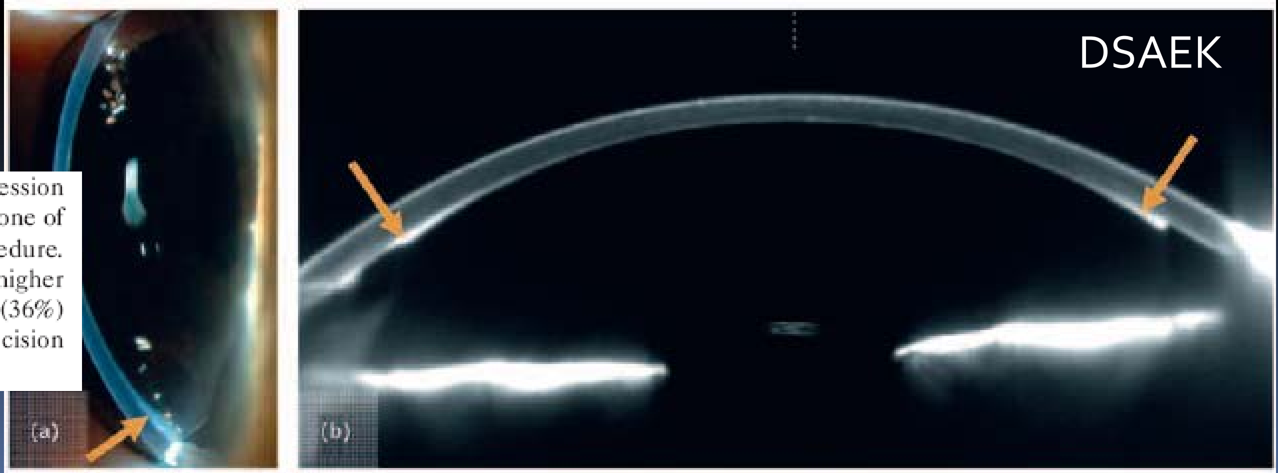


Diagram displaying (a) DSEK/DSAEK and (b) DMEK procedures. In both techniques, the recipient Descemet membrane is excised by descemetorhexis. In DSEK/DSAEK, a donor posterior lamellar disk consisting of posterior stroma, Descemet membrane, and its endothelium is transplanted, whereas in DMEK only an isolated donor Descemet membrane with its endothelium is transplanted. In DSEK, donor stromal dissection is performed manually, and in DSAEK, with the use of a microkeratome. In DMEK, the donor Descemet membrane is stripped off from a corneoscleral button. DMEK, Descemet membrane endothelial keratoplasty; DSAEK, Descemet stripping automated endothelial keratoplasty; DSEK, Descemet stripping endothelial keratoplasty.





Several studies [21•,47,48] have shown that compression of the donor lenticule during the insertion may be one of the most traumatic steps during the surgical procedure. In DSAEK, endothelial cell damage may be higher with 'trifolded' grafts through a 3-mm incision (36%) than 'bifolded' taco lenticules through a 5-mm incision (19%) [47].

Comparison of Central Corneal Graft Thickness to Visual Acuity Outcomes in Endothelial Keratoplasty

Kristiana D. Neff, MD, Joseph M. Biber, MD,†‡ and Edward J. Holland, MD†‡*

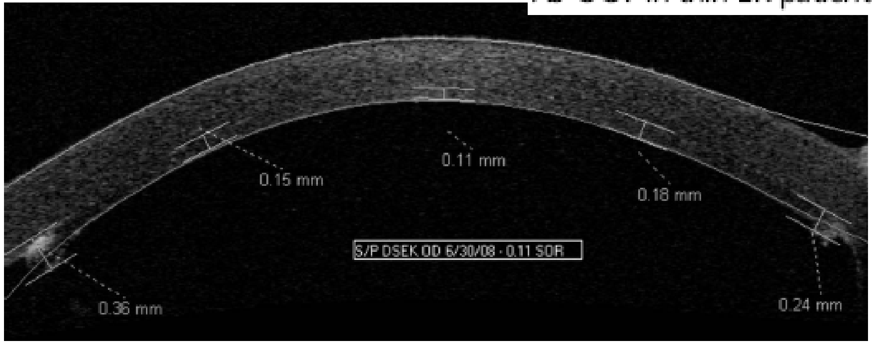
Cornea 2011;30:388–391

Purpose: To evaluate visual acuity outcomes after endothelial keratoplasty (EK) and describe the relationship to postoperative central corneal graft thickness as measured by anterior segment optical coherence tomography (AS-OCT).

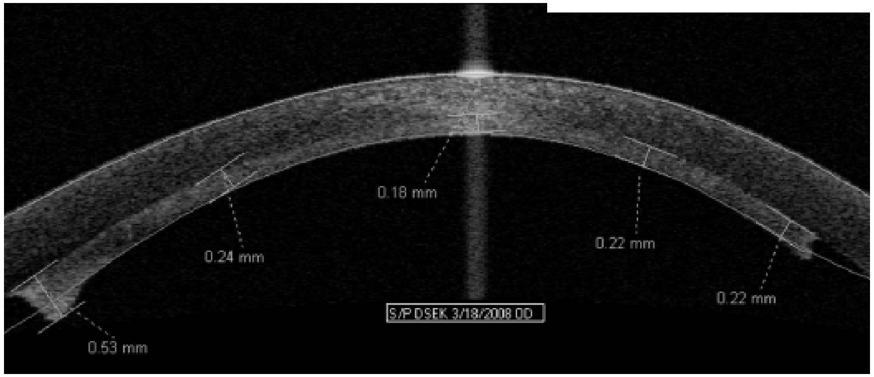
EK has become the preferred procedure for the surgical treatment of endothelial dysfunction. Our results demonstrate that thin EK results in better visual acuity. This idea is further supported by current research to perfect the "ultrathin" lamellar keratoplasty, Descemet membrane EK. Our excellent visual acuity results with thin EK allow one to ask how thin the posterior donor disks need to be to maximally optimize visual acuity outcomes. Further studies need to be done to look at the differences in both visual acuity and endothelial cell loss with thin EK versus Descemet membrane EK. With our data in mind, we propose that surgeons consider using thinner tissue to optimize visual results in EK.

Conclusions: Thin EK versus thick EK, as measured by AS-OCT in the postoperative period, showed a statistically significant improvement in BSCVA.

AS-OCT in thin EK patient.

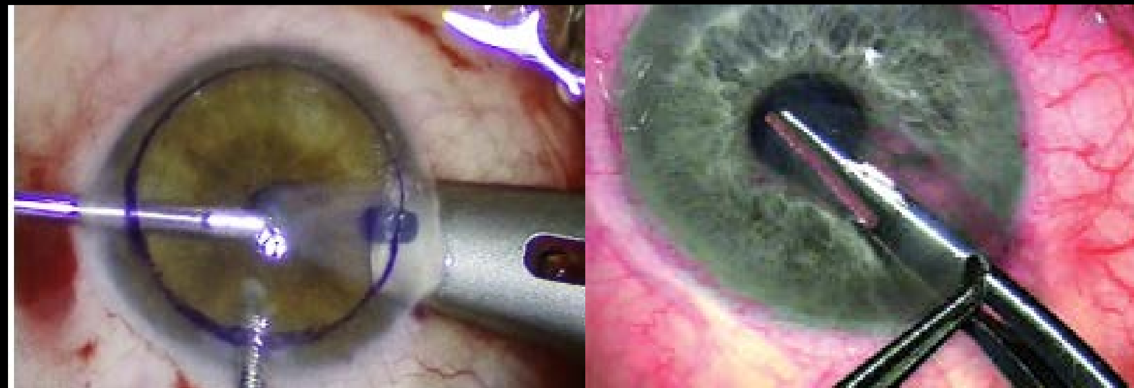


AS-OCT in thick EK

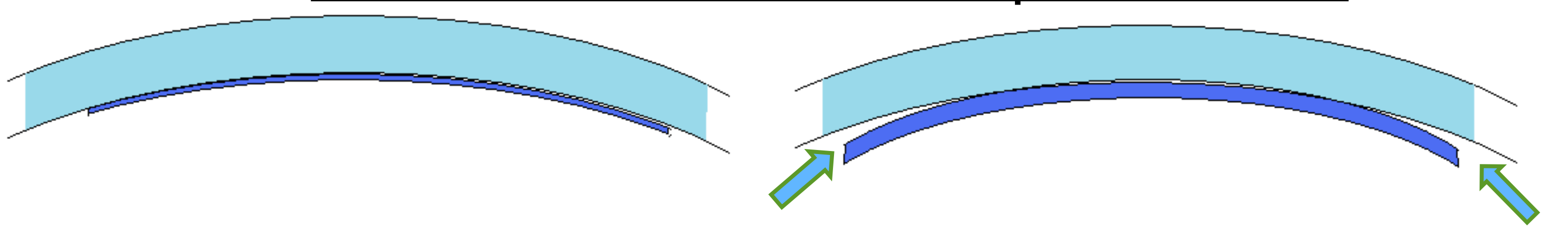


Why an ultrathin DSAEK?

Donor insertion



Mismatch between donor and recipient curvatures

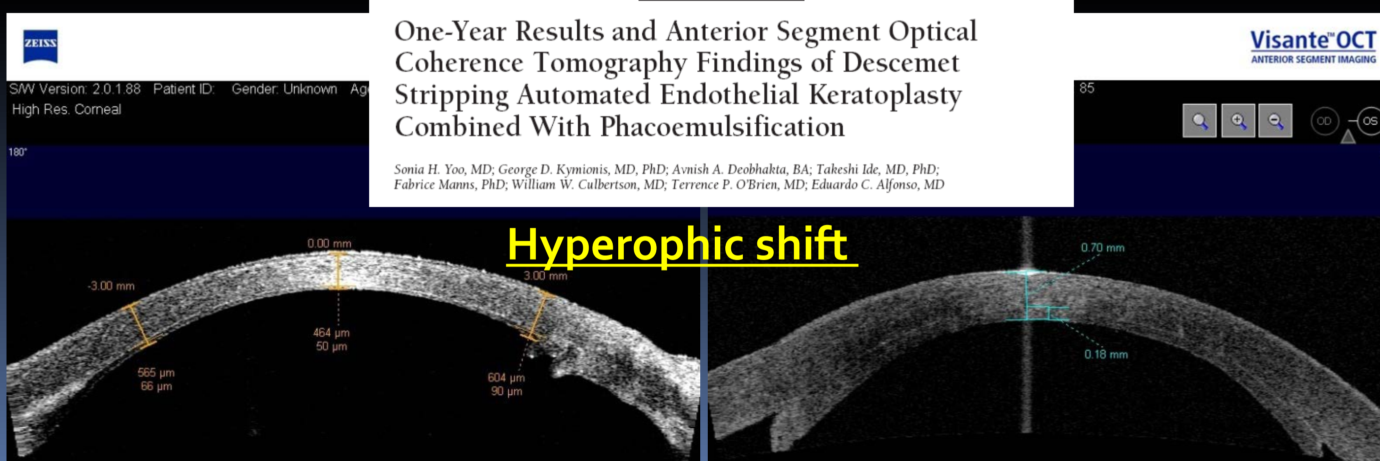


CLINICAL SCIENCES
Arch Ophthalmol. 2008;126(8):1052-1055

One-Year Results and Anterior Segment Optical Coherence Tomography Findings of Descemet Stripping Automated Endothelial Keratoplasty Combined With Phacoemulsification

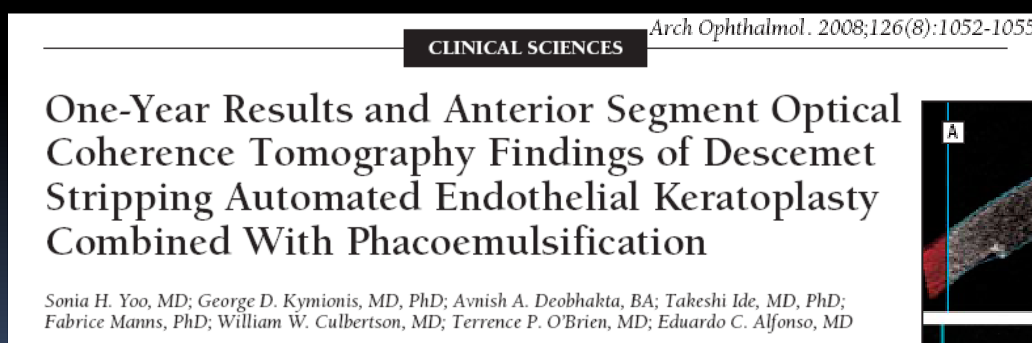
Sonia H. Yoo, MD; George D. Kymionis, MD, PhD; Avnish A. Deobhakta, BA; Takeshi Ide, MD, PhD; Fabrice Manns, PhD; William W. Culbertson, MD; Terrence P. O'Brien, MD; Eduardo C. Alfonso, MD

Hyperophic shift



OCT visante evaluation

preoperative evaluation



CLINICAL SCIENCES

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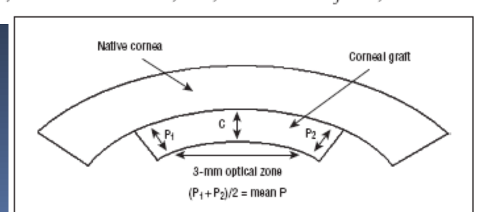
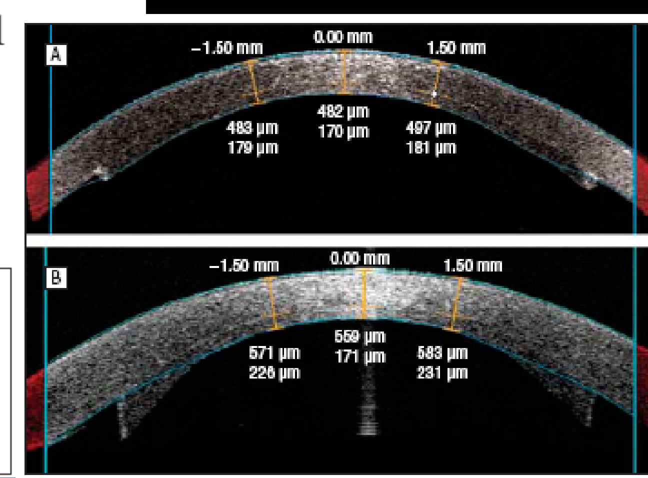
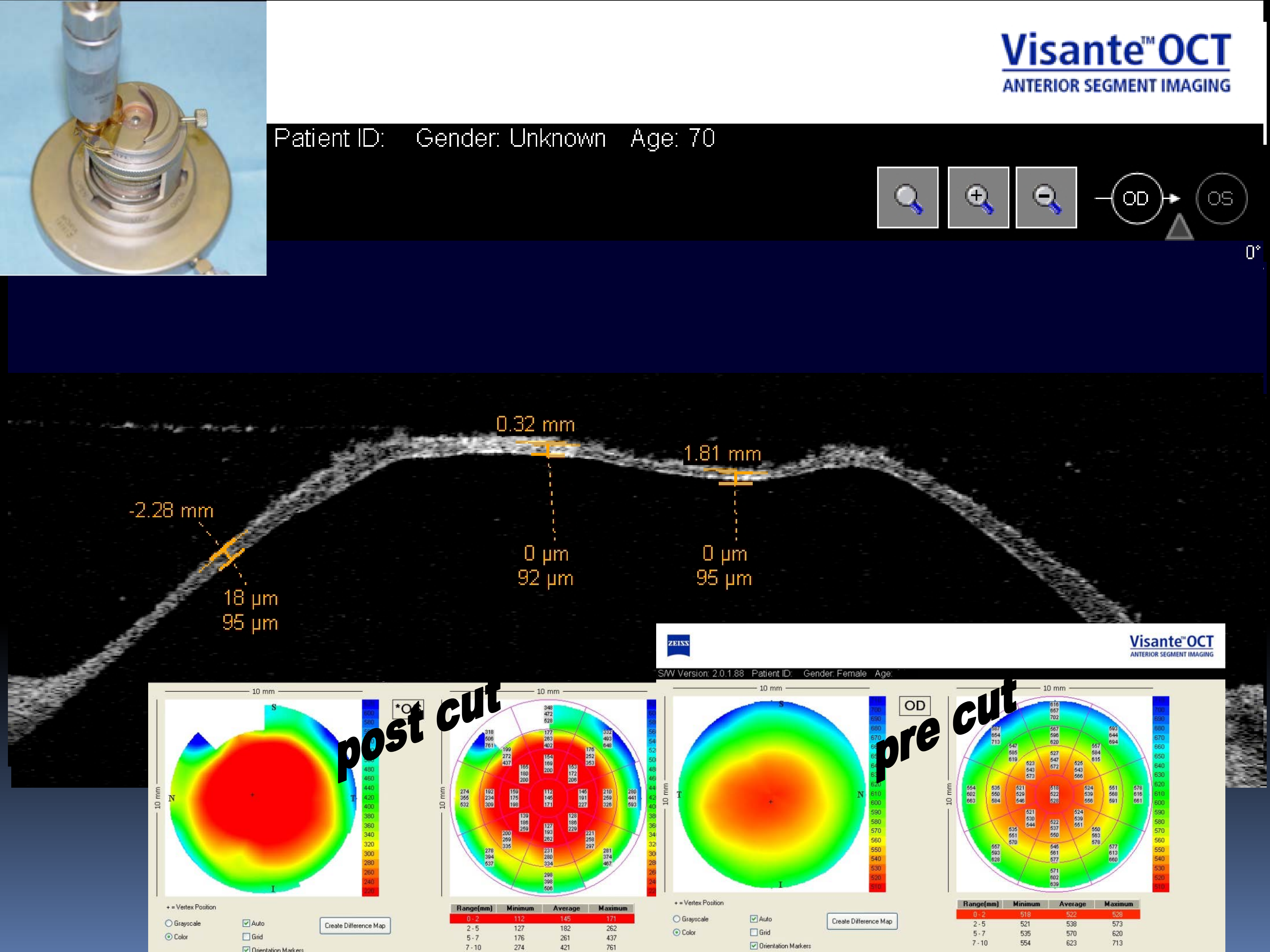


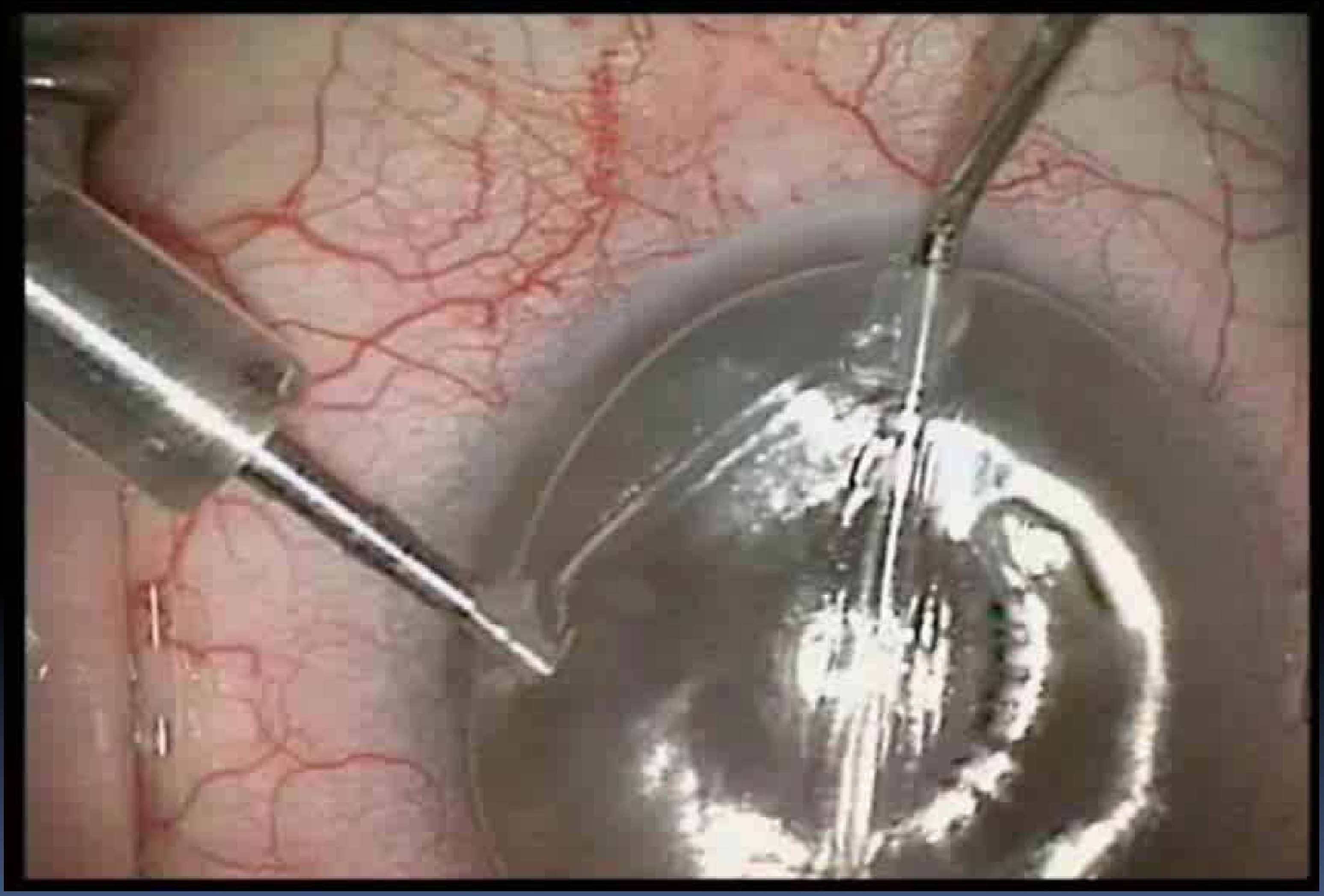


postoperative evaluation

Precut tissue in eye bank


Visante™ OCT
ANTERIOR SEGMENT IMAGING
Patient ID: Gender: Unknown Age: 70
OD
OS
0°
0.32 mm
1.81 mm
-2.28 mm
0 µm
92 µm
0 µm
95 µm
18 µm
95 µm
post cut
pre cut
ZEISS
Visante™ OCT
ANTERIOR SEGMENT IMAGING
S/W Version: 2.0.1.88 Patient ID: Gender: Female Age:
10 mm
S
N
T
I
OD
+ = Vertex Position
Grayscale
Color
Auto
Grid
Orientation Markers
Create Difference Map
Range(mm) Minimum Average Maximum
0 - 2 112 145 171
2 - 5 127 182 262
5 - 7 176 261 437
7 - 10 274 421 761
Range(mm) Minimum Average Maximum
0 - 2 518 522 528
2 - 5 521 538 573
5 - 7 535 570 620
7 - 10 554 623 713

Ultra-thin DSAEK



Effect of Incision Width on Graft Survival and Endothelial Cell Loss After Descemet Stripping Automated Endothelial Keratoplasty

Marianne O. Price, PhD,† Maria Bidros, MD,‡ Mark Gorovoy, MD,§ Francis W. Price, Jr, MD,*† Beth A. Benetz, CRA, MA,‡ Harry J. Menegay, PhD,‡ Sara M. Debanne, PhD,¶ and Jonathan H. Lass, MD‡¶*

Cornea 2010;29:523–527

Purpose: To assess the effect of incision width (5.0 and 3.2 mm) on graft survival and endothelial cell loss 6 months and 1 year after Descemet stripping automated endothelial keratoplasty (DSAEK).

Conclusions: One year after DSAEK, overall graft success was comparable for the 2 groups; however, the 5.0-mm incision width resulted in substantially lower endothelial cell loss at 6 and 12 months.

Despite these limitations, given the significant and greater than 10% difference in endothelial cell loss between the groups at both 6- and 12-month postoperative time points, we feel confident that the use of a 5.0-mm incision width is associated with significantly lower 6- and 12-month endothelial cell loss than the use of a smaller 3.2-mm incision width for forceps insertion of folded DSAEK grafts. Despite this difference in cell loss, the early 1-year graft survival rates were comparable, and thus, additional follow-up is needed to determine whether the larger incision has an advantage over the smaller incision in terms of long-term graft survival.

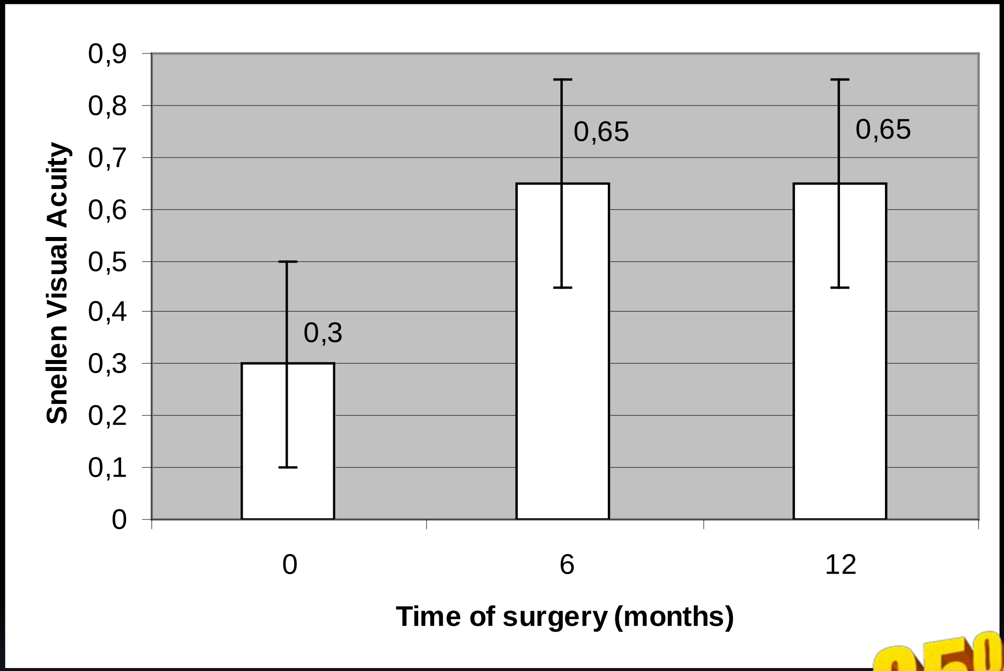
TABLE 3. Endothelial Cell Density and Cell Loss for DSAEK Performed at 2 Sites

ECD (Cells/mm^2)	Site A, Mean (SD)	No. Eyes	Site B, Mean (SD)	No. Eyes	*P*
Baseline	2780 (294)	64	2780 (311)	103	0.97
6 mo	2050 (578)	55	1650 (618)	71	<0.001
12 mo	1940 (570)	45	1580 (635)	62	<0.001
Endothelial Cell Loss (%)	Mean (SD) (Maximum Loss) (Minimum Loss)		Mean (SD) (Maximum Loss) (Minimum Loss)		
6 mo	27 (20) (−67%) (+23%)	55	40 (22) (−81%) (−1%)	71	<0.001
12 mo	31 (19) (−70%) (+25%)	45	44 (22) (−80%) (+4%)	62	<0.001

Results

BCVA (Snellen)

All our patients (31) improved the visual acuity at the end of the follow-up



Pre-op BCVA

Mean BCVA 0,25 ± 0,2

Post- op BCVA

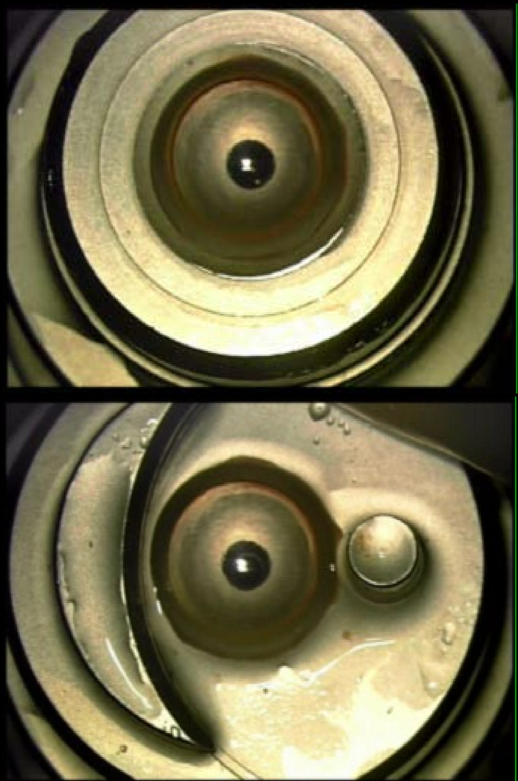
6 months fw 0,65 ± 0,2 (31 cases)

12 months fw 0,65 ± 0,23 (31 cases)

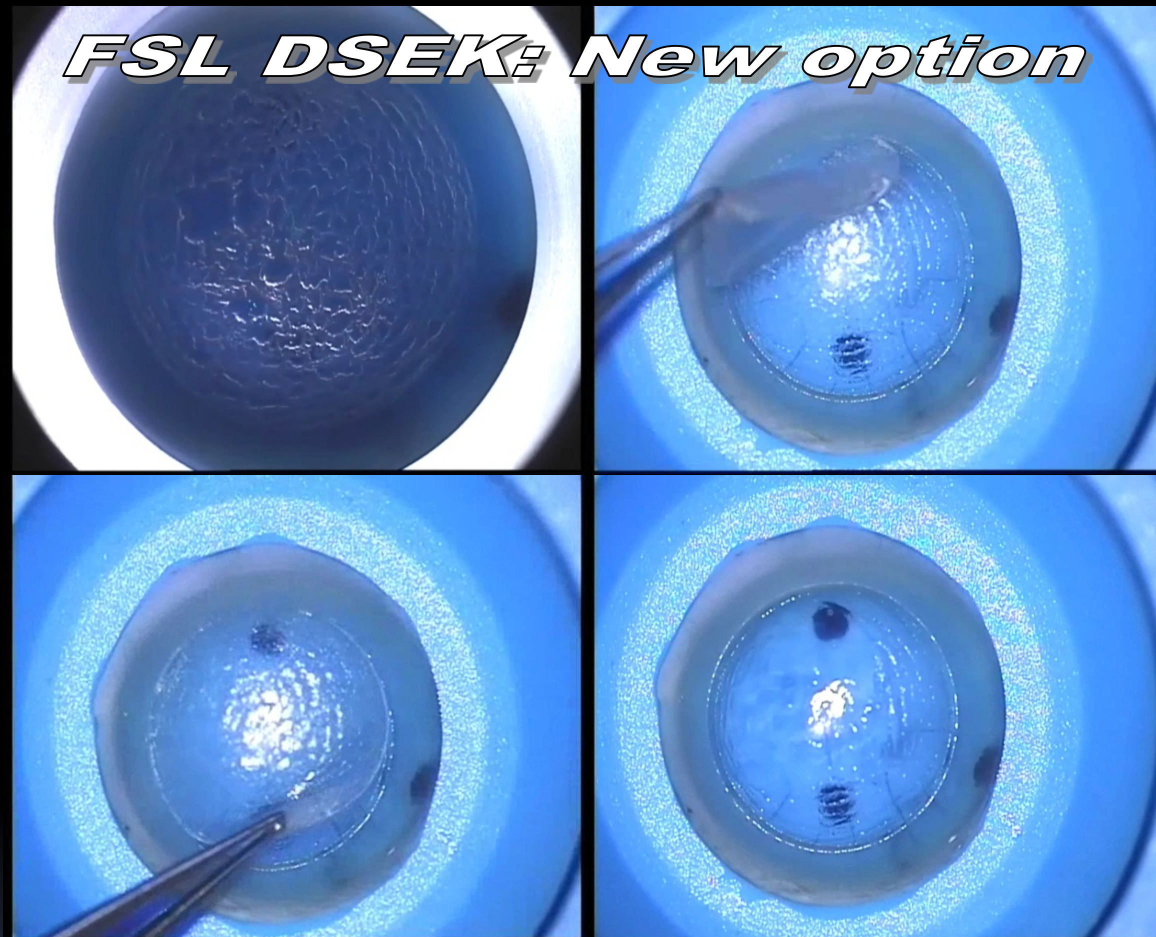
12 months fw excluding comorbidity 0,67 ± 0,22 (25 cases)

ECD loss 35%

At 6 months after surgery, BCVA was improved in all eyes (100%).
At 12 months a further improvement has been recorded excluding comorbidity.
In 7/31 (22,6%) patients 1,0 BCVA was reached at 12 months.



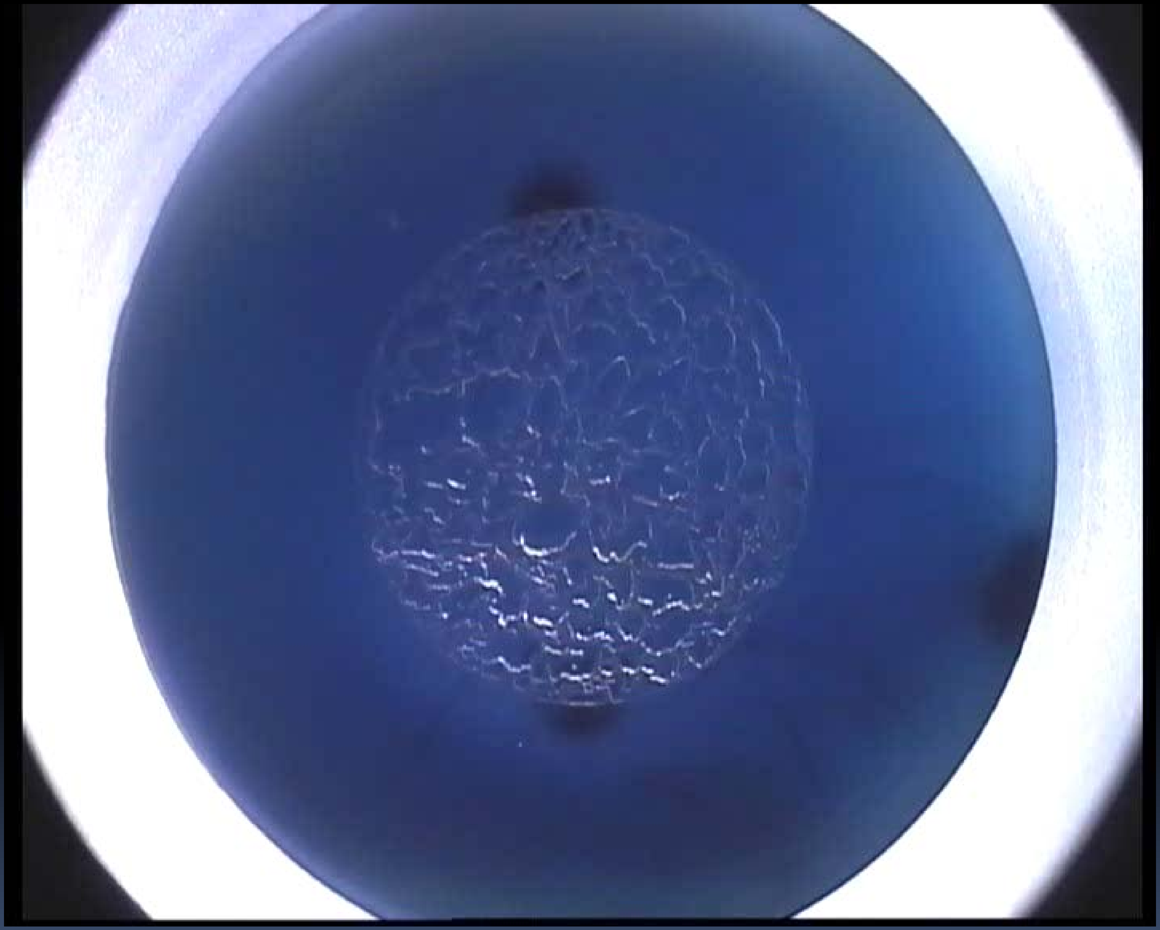
MK DSAEK:
Gold standard



Descemet stripping automated EK is currently the most widely used method For endothelial transplantation.

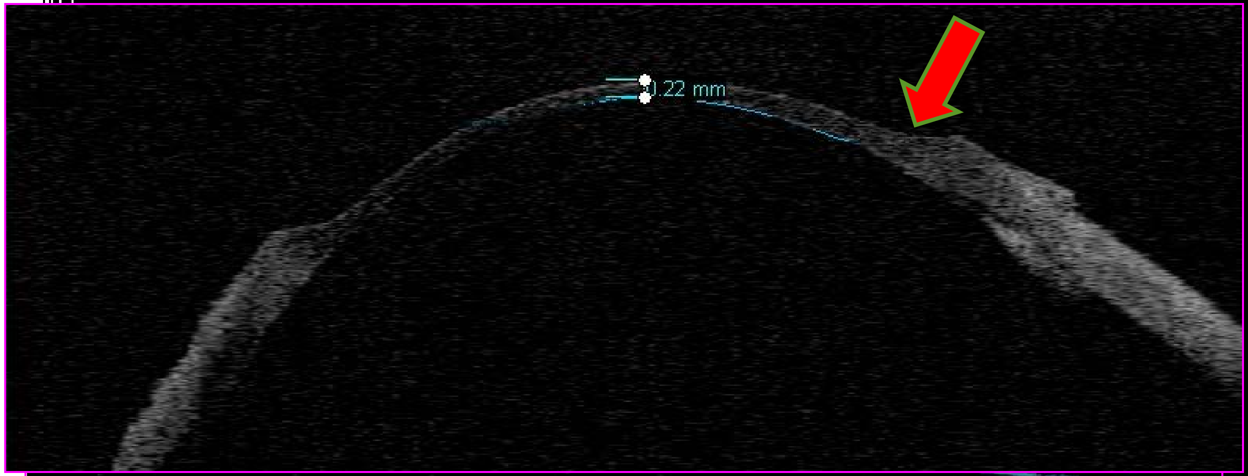
Price and Price. Clin Experiment Ophthalmol 2010

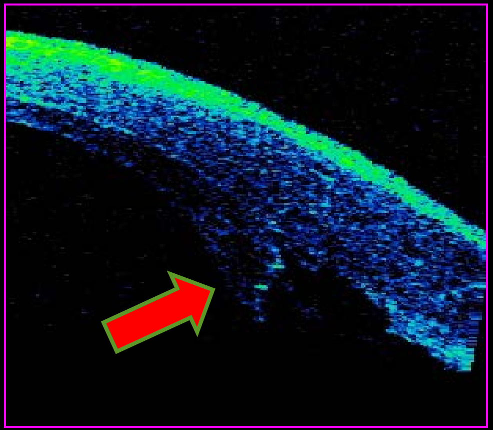
FSL deep stromal dissections: DSAEK lenticule creation

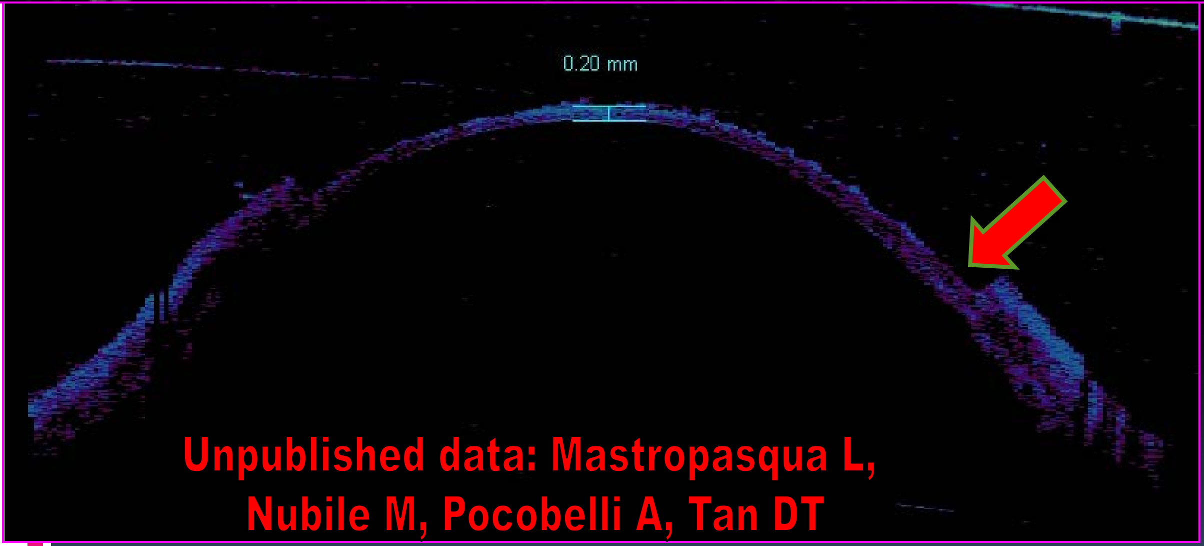


500 Khz FSL - 450 microns depth
9.00 mm diameter

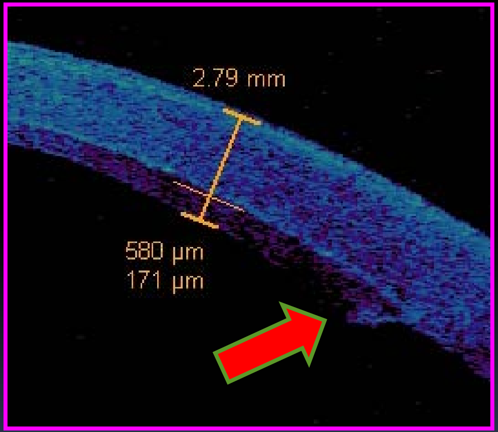
OCT imaging of the cornea to calculate dissection profiles and thicknesses in posterior lamellar keratoplasty





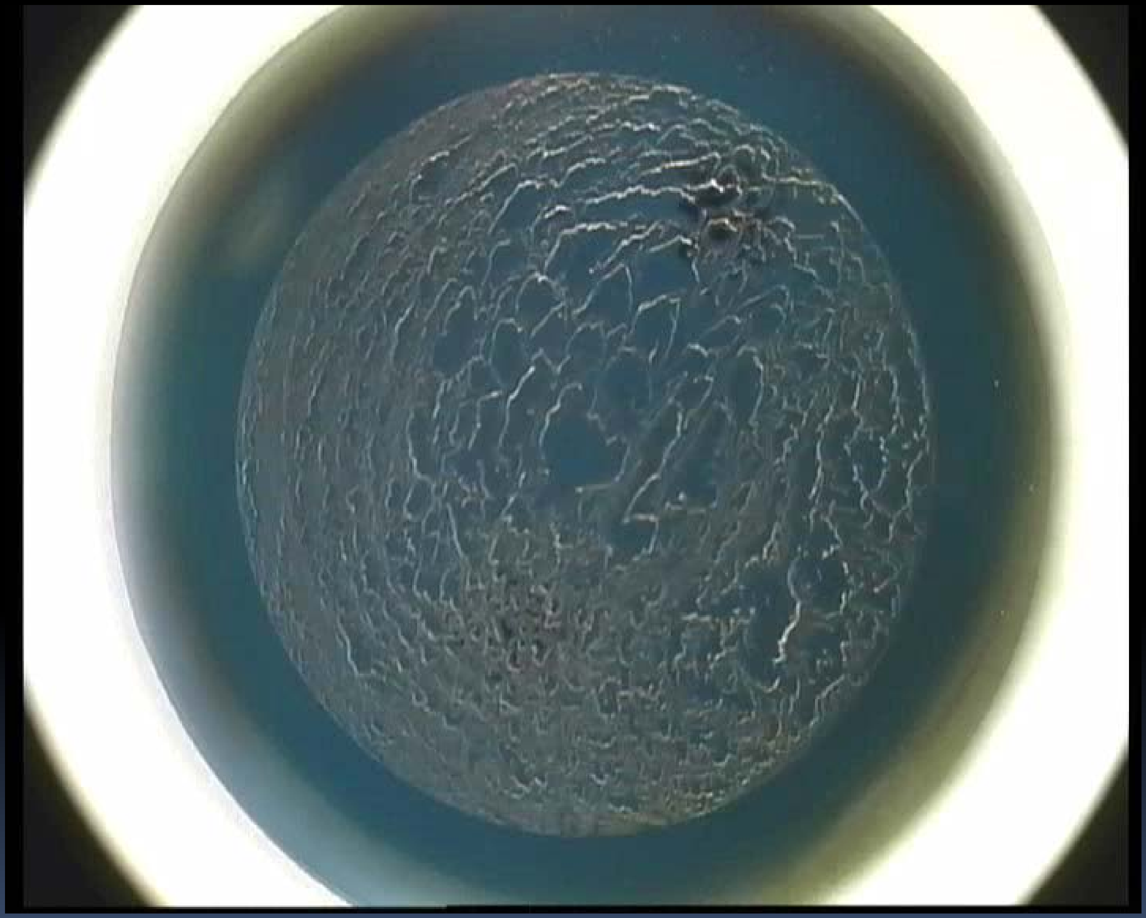


Unpublished data: Mastropasqua L, Nubile M, Pocobelli A, Tan DT

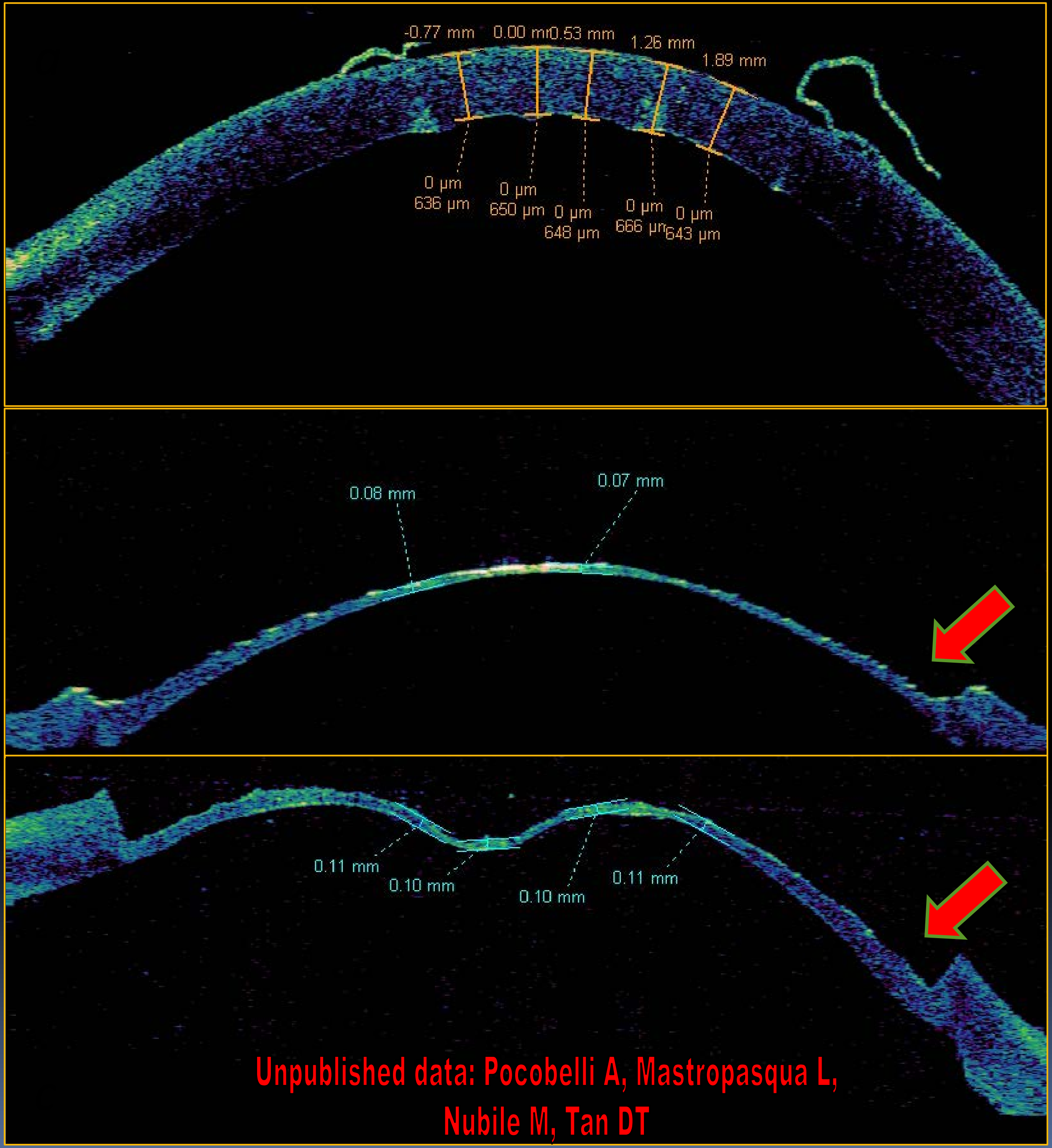


More predictable PLD thickness
And regular profile in the periphery
In FSL dissections

FSL deep stromal dissections: Ultra-thin DSAEK lenticule creation



Ultra-thin FSL - DSEK



Unpublished data: Pocobelli A, Mastropasqua L, Nubile M, Tan DT

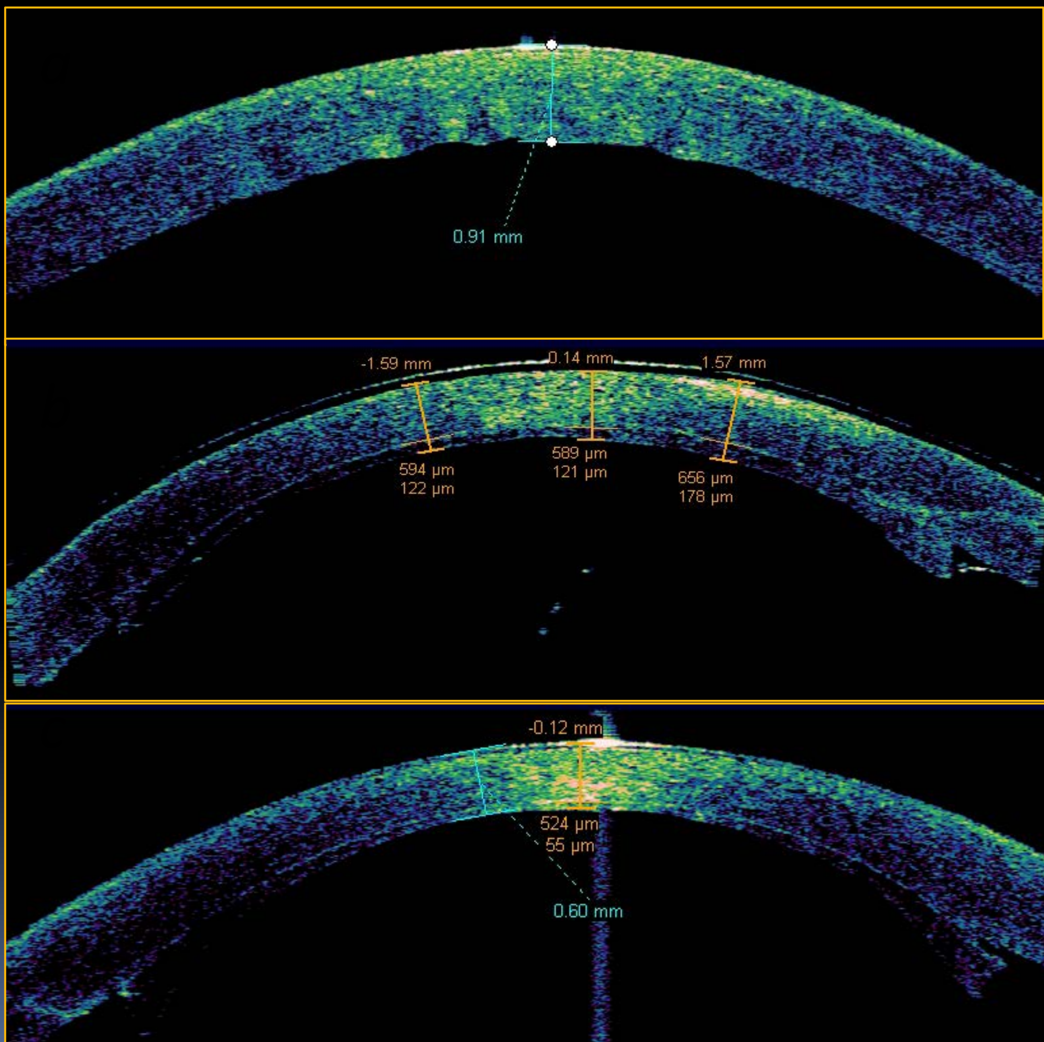
a) AS-OCT average pachymetry of donor cornea: 650 microns

b) AS-OCT pachymetry Of posterior residual stroma after: 550 microns FSL dissection 75 microns in AC

c) AS-OCT pachymetry Of posterior residual stroma after: 550 microns FSL dissection 100 microns free

Ultra-thin FSL - DSEK

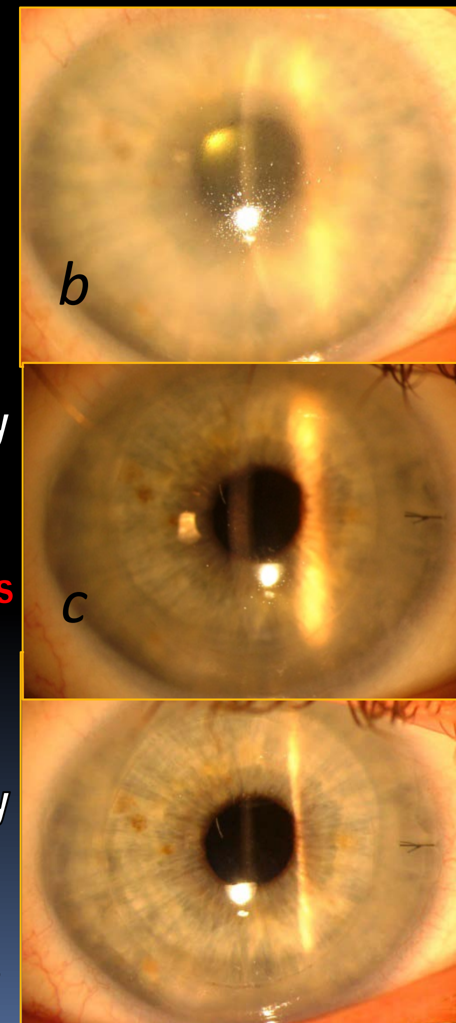
-Clinical example: Massive corneal oedema due to toxic anterior segment syndrome



a) OCT pachymetry of preop cornea: 910 microns

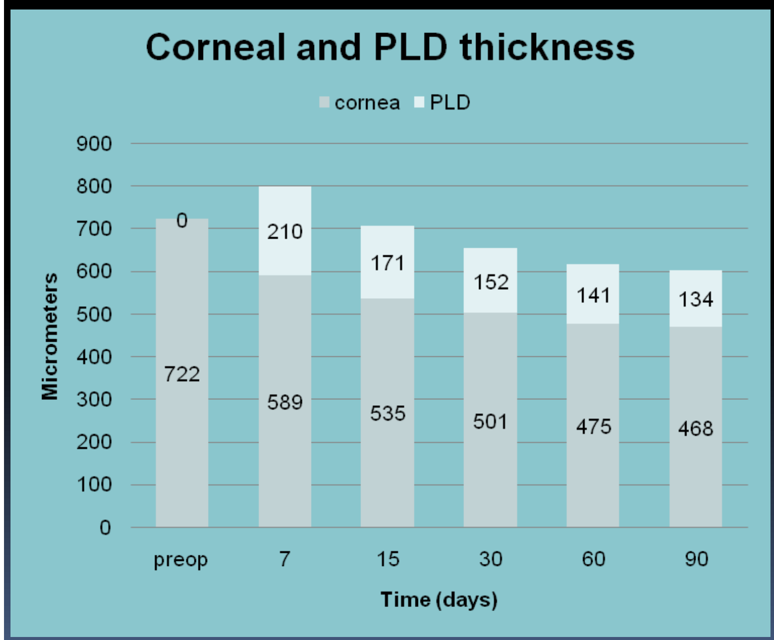
b) OCT pachymetry host cornea PLD 120 µm at 48 hours

c) OCT pachymetry host cornea PLD 55 µm at 2 weeks



Litterature review on FSL - DSEK

FSL	Author	Journal	N. of eyes	Mean BCVA	EC loss	Graft thickness
30 KhZ	Cheng YY	Transplantation 2009	36	20/70	65%	117
30 KhZ	Cheng YY	Arch Ophthal 2008	20	20/57	48%	-
60 KhZ	Monterosso C	Cornea 2011	4	20/50	-	150



	Mean ± SD	Range
ECD (cells/mm2)		
Donor	2630 ± 131	2320-2750
1 Mo	1255 ± 344	950-1622
3 Mo	1206 ± 361	894-1530
6 Mo	1192 ± 327	802-1466
Endothelial cell loss		
6 mo vs donor (%)	54 ± 13	35-74

Our case series (200-500 KhZ). 14 eyes (mean BCVA 20/50)

Interface quality of endothelial keratoplasty buttons obtained with optimised femtosecond laser settings

Antoine Rousseau,[1] Abdelkader Bensalem,[2] Virginie Garnier,[3] Michèle Savoldelli,[1,4] Jean-Jacques Saragoussi,[1,5] Gilles Renard,[6] Jean-Louis Bourges[6]

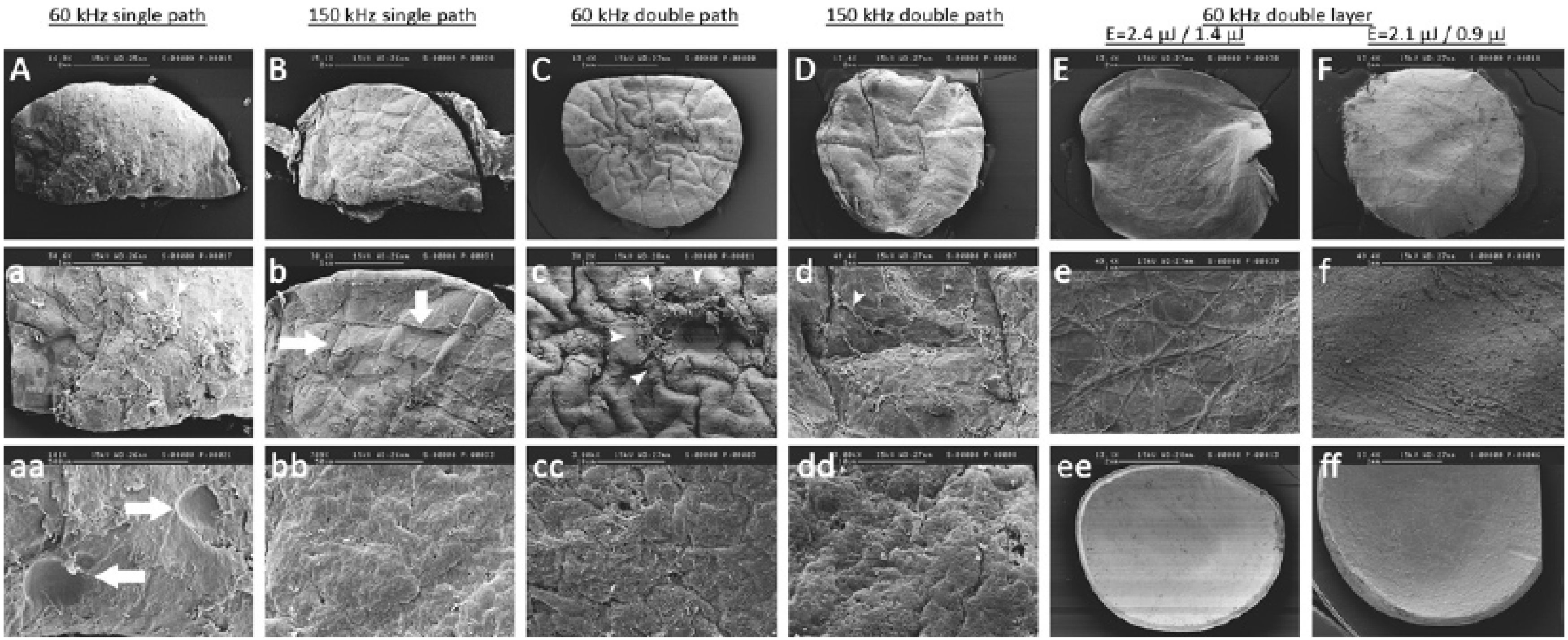


Figure 3 Interfaces created with an Intralase femtosecond Laser and observed by SEM after various full lamellar cut profiles. After a full lamellar cut set with a single path and a posterior side cut in group 1 (A, a, aa) and 2 (B, b; bb), the endothelial lenticule displayed marked central and peripheral collagen irregularities owing to adherences (a; arrowheads) associated with sparse hollows (a; white arrows) or straight crossing lines (b; white arrows). After a double path procedure in groups 3 (C, c, cc) and 4 (D, d, dd), collagen irregularities, although still visible in the central area of the lenticule (c and d; arrowheads), were less marked in group 4 (d) compared with group 3(c). After two successive cuts in group 5, energy set either at 2.4/1.4 µJ (E, e, ee) or at 2.1/0.9 µJ (F, f, ff), both the mid-stromal interface (ee, ff) and the posterior stromal interface of the lenticule were smooth and free of irregularities (e, f). The lenticule interfaces were smoother when created with 0.9 µJ (f) than with 1.4 µJ (e).

"Ultrathin" DSAEK Tissue Prepared With a Low–Pulse Energy, High-Frequency Femtosecond Laser

Paul M. Phillips, MD, Louis J. Phillips, OD,* Hisham A. Saad, MD,† Mark A. Terry, MD,‡§ Donna B. Stolz, PhD,¶ Christopher Stoeger, CEBT,§ Jonathan Franks, PhD,¶ and David Davis-Boozer, MPH§*

Cornea 2012

Purpose: To evaluate the endothelial cell survival and stromal bed quality when creating deep stromal cuts with a low–pulse energy, high-frequency femtosecond laser to produce "ultrathin" tissue for Descemet stripping automated endothelial keratoplasty.

Methods: Seventeen corneas were used for this study. Five corneas were cut with the laser at a depth of 420 to 500 μm to produce a tissue thickness of approximately ≤70 μm. Five corneas served as an uncut comparison group. Vital dye staining and computer

Conclusions: Ultrathin tissue for Descemet stripping automated endothelial keratoplasty can be safely prepared with minimal endothelial cell damage using a low–pulse energy, high-frequency femtosecond laser; however, the resulting stromal surface quality may not be optimal with this technique.

In conclusion, the use of the LPEHF laser to create ultrathin DSAEK tissue holds promise, as seen in our study, that this laser can reliably create ultrathin DSAEK tissue without causing significant damage to the delicate endothelium. Modification of energy settings and cutting techniques may improve the final stromal bed quality, which should be the focus of future studies.

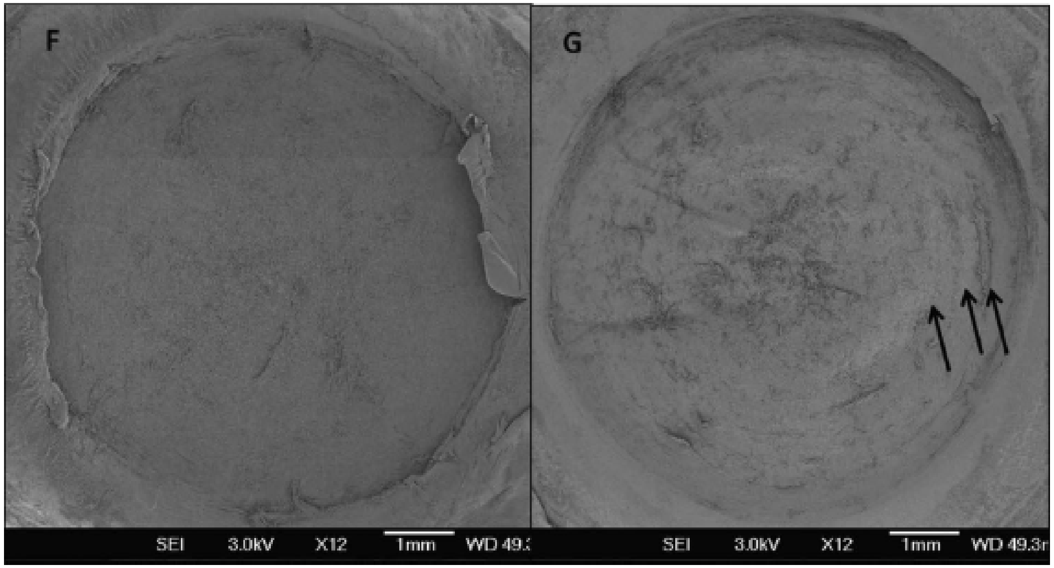
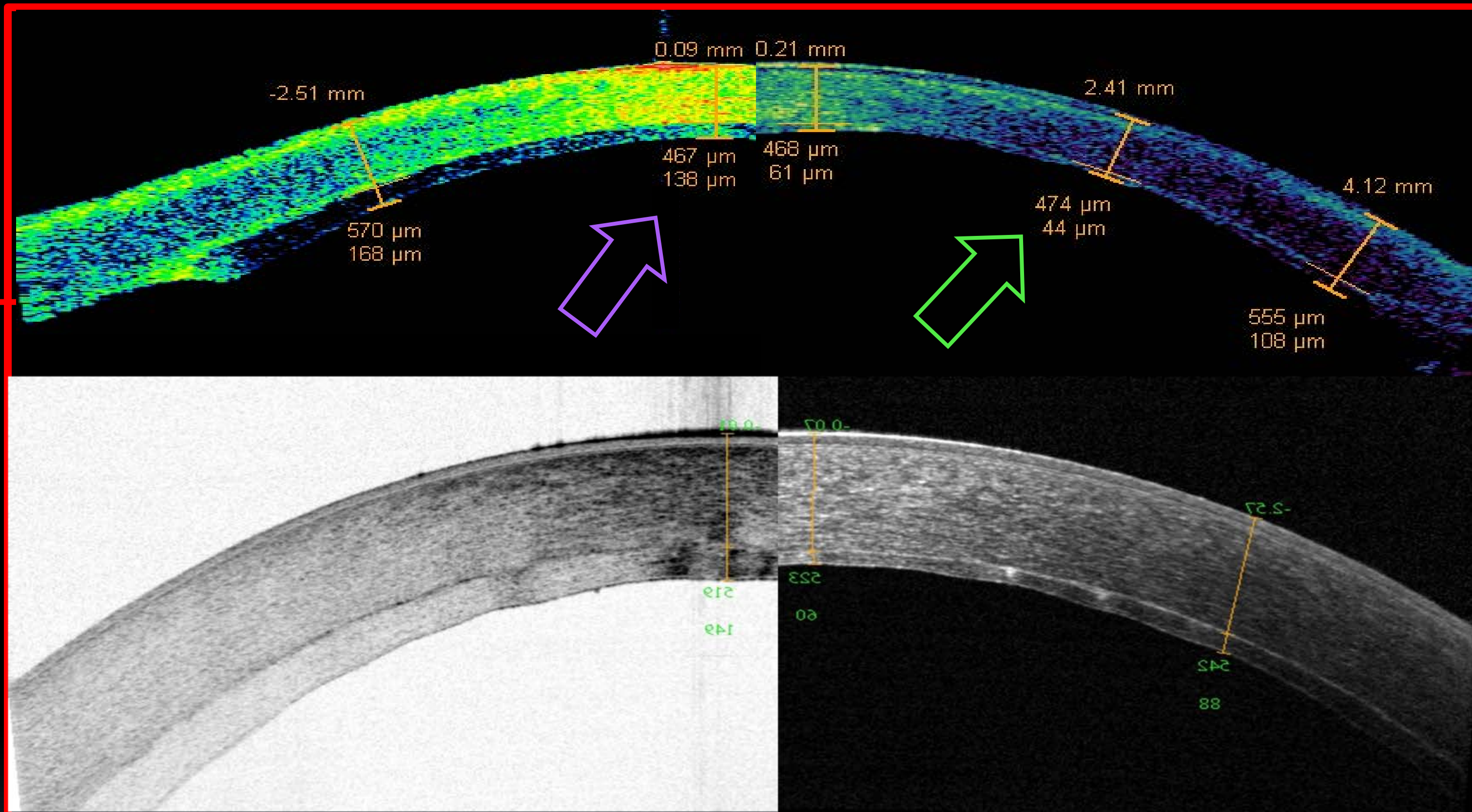


FIGURE 2. SEM low-magnification (×12) postlaser images demonstrating an example of a generally smooth bed (cornea F) as compared with a rougher bed with characteristic concentric ring (arrows) formation (cornea G).

Do we have advantages with FSL EK (Ultra-thin)?



DSEK procedure with Predictable PLD thickness

More physiological postop morphology/thickness

Alternative to DMEK (?)

Costs!!

Endothelial count?

Complications rate?

Visual results?

Economic Evaluation of Endothelial Keratoplasty Techniques and Penetrating Keratoplasty in The Netherlands

FRANK J.H.M. VAN DEN BIGGELAAR, YANNY Y.Y. CHENG, RUDY M.M.A. NUIJTS, JAN S.A.G. SCHOUTEN, ROBERT-JAN WIJDH, ELISABETH PELS, HUGO VAN CLEYNENBREUGEL, CATHARINA A. EGGINK, WILHELMINA J. RIJNEVELD, AND CARMEN D. DIRKSEN

(Am J Ophthalmol 2012

• PURPOSE: To evaluate cost-effectiveness of penetrating keratoplasty (PK), femtosecond laser-assisted Descemet stripping endothelial keratoplasty (FS-DSEK), and Descemet stripping automated endothelial keratoplasty (DSAEK).

The results of this study show that FS-DSEK was not cost-effective compared to PK and DSAEK. DSAEK, on the other hand, was more costly and also more effective, resulting in an ICER of €4975 (US$5920) per clinically improved patient. It depends on the threshold value for cost-effectiveness whether DSAEK or PK is the preferred technique. Within a broad range of threshold values both DSAEK and PK might be cost-effective. However, preparing lamellar transplant buttons in a national cornea bank can significantly lower the costs per patient in the DSAEK group, which could improve the cost-effectiveness of DSAEK and could lower the uncertainty around the ICERs. Studies with a longer

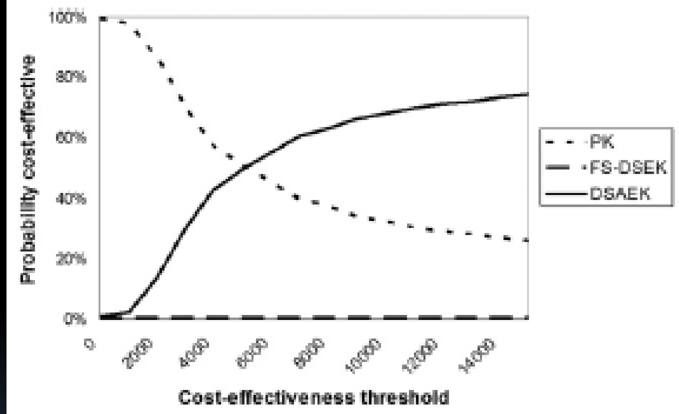


FIGURE. Cost-effectiveness acceptability curves for the incremental costs per clinically improved patient for penetrating keratoplasty (PK), femtosecond laser–assisted Descemet stripping endothelial keratoplasty (FS-DSEK), and Descemet stripping automated endothelial keratoplasty (DSAEK). The curve shows the probability (vertical axis) of which technique is cost-effective over a range of values for the maximum acceptable ceiling ratio (horizontal axis).

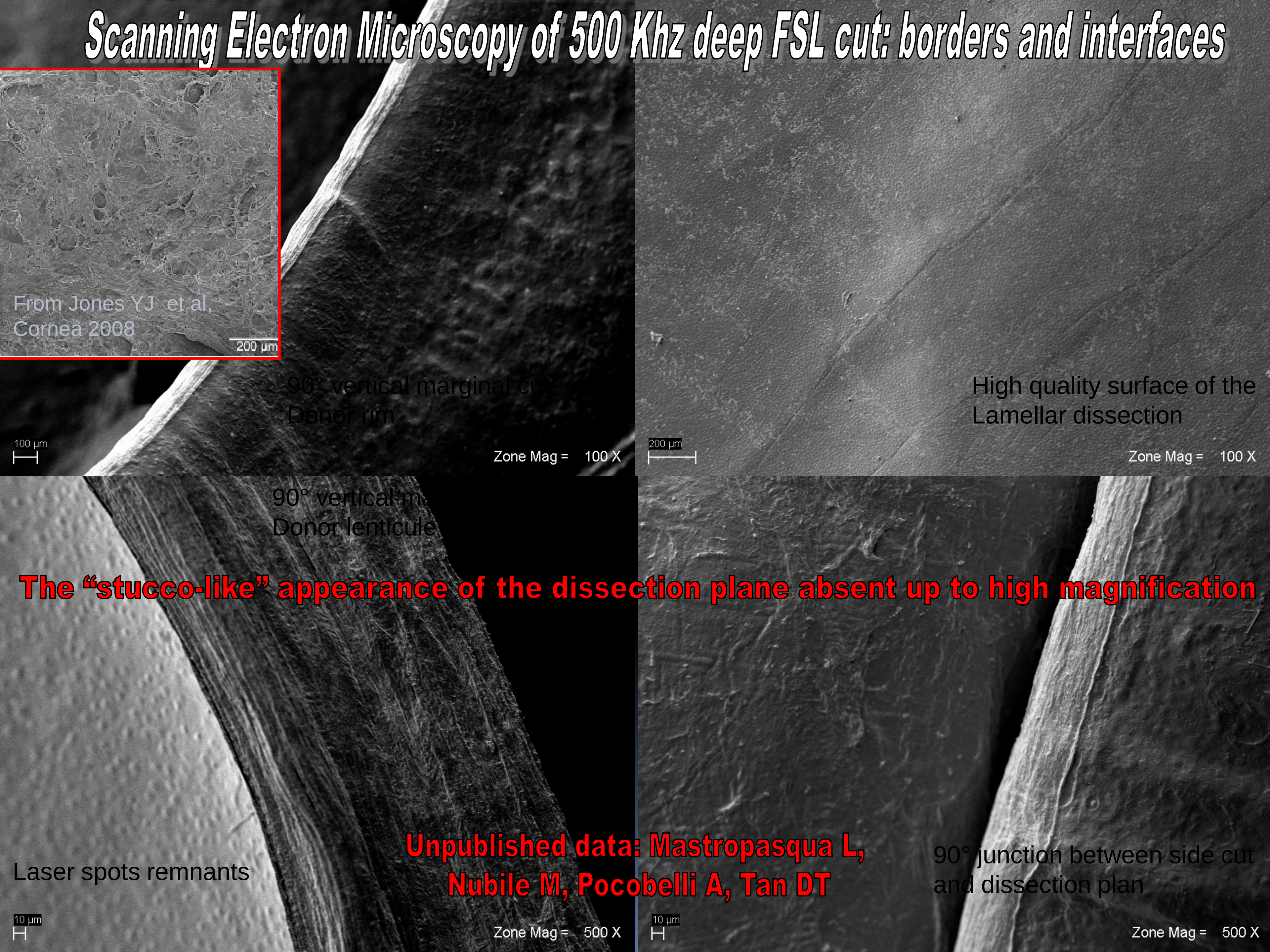
Document	Technical Guidelines for Ocular Tissue (TGOT)
Revision	5 (draft)
Page	2 of 9
Operative from	t.b.c.

2 PROCESSING AND STORAGE OF CORNEAL TISSUE.

2.1 General.

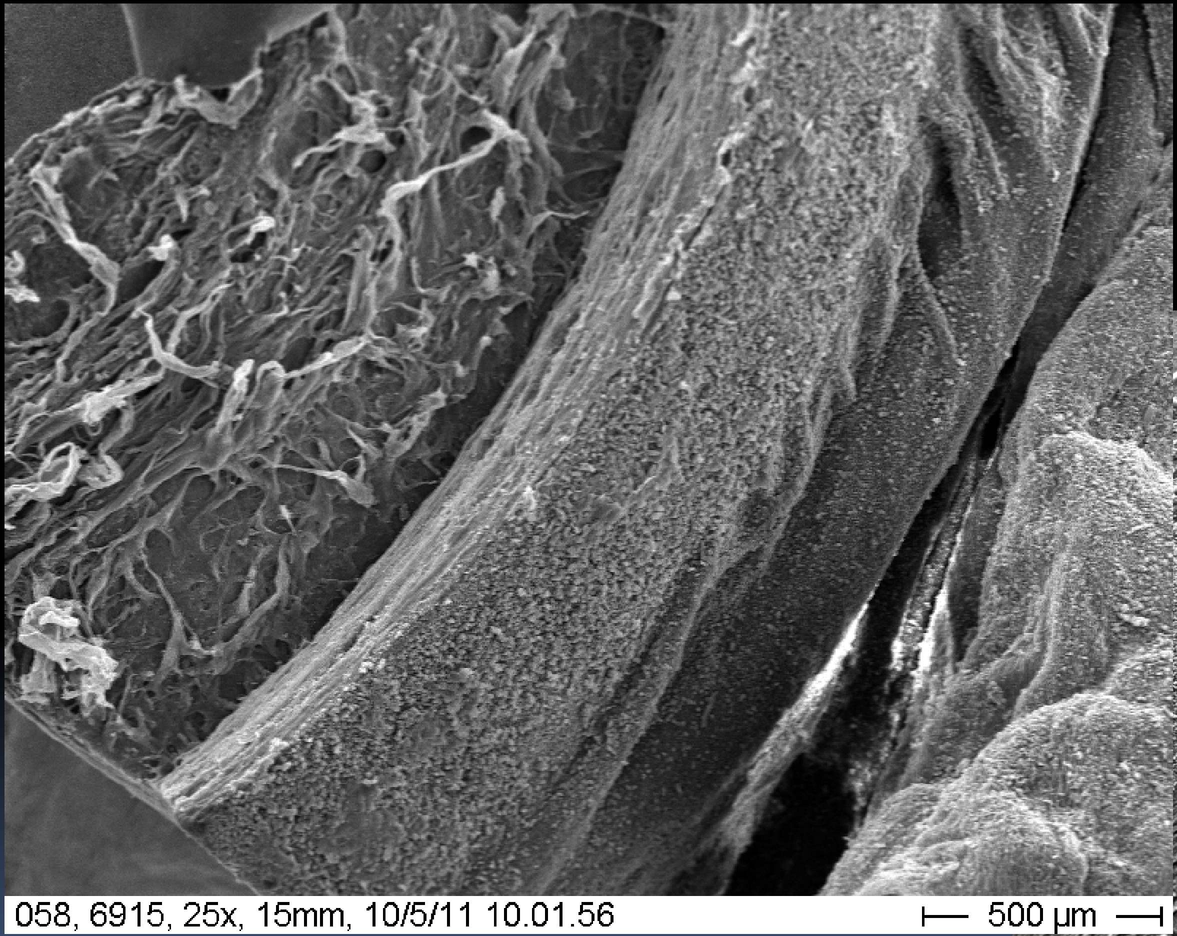
- Use only reagents and materials from suppliers that meet the documented requirements and specifications approved by the Responsible Person / Medical Director. CE/pharmacopeia-labelled materials/chemicals are recommended.
- All procedures must be documented in SOPs, including method and dates for decontamination, endothelial evaluation and microbiological testing of the tissue. Time point is documented if necessary.
- ~~Use aseptic techniques while processing the tissue in the eye bank.~~
- ~~The required air quality standard of the environment (air particle/CFU-count) in which the corneal tissue will be proce~~ssed should be defined and monitored (usually class A in class D background).
- Considering that:
  - post-mortem eye tissue is generally contaminated,
  - the amount of remaining contaminating microbes is dependent on pre-storage decontamination procedures, antibiotics during storage, and storage

THANK YOU FOR YOUR ATTENTION

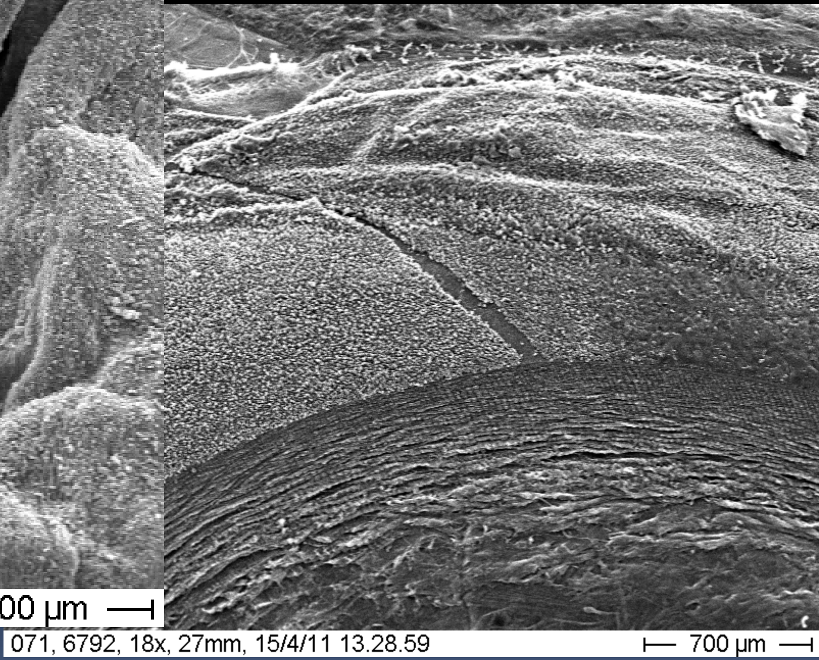

Scanning Electron Microscopy of 500 Khz deep FSL cut: borders and interfaces
From Jones YJ et al, Cornea 2008
200 µm
90° vertical marginal
Donor rim
100 µm
Zone Mag = 100 X
High quality surface of the Lamellar dissection
200 µm
Zone Mag = 100 X
90° vertical
Donor lenticule
The "stucco-like" appearance of the dissection plane absent up to high magnification
Laser spots remnants
10 µm
Zone Mag = 500 X
Unpublished data: Mastropasqua L, Nubile M, Pocobelli A, Tan DT
90° junction between side cut and dissection plan
10 µm
Zone Mag = 500 X

Unpublished data A.Pocobelli, R. Colabelli, P. Ducoli, L . Pannarale

SEM

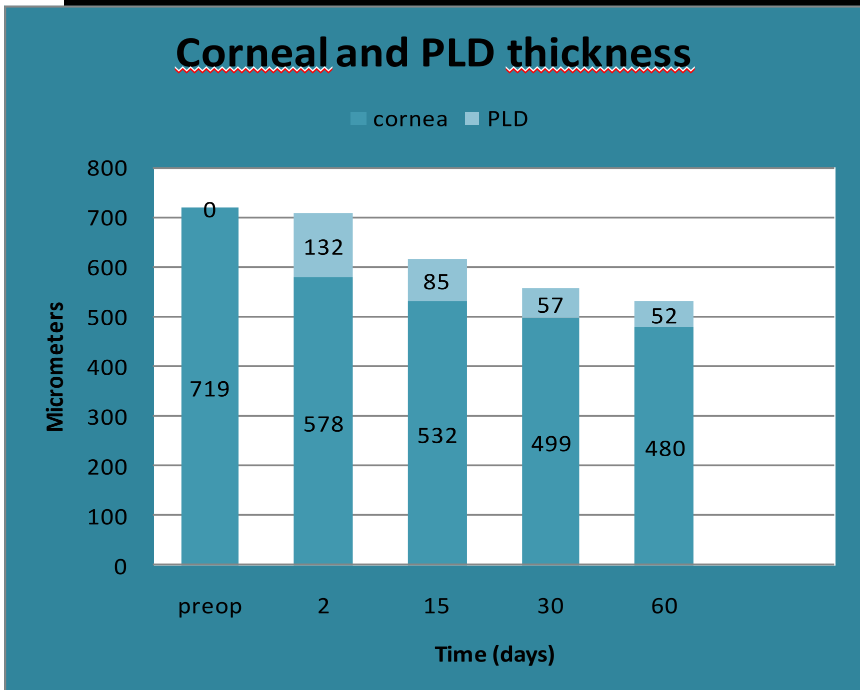


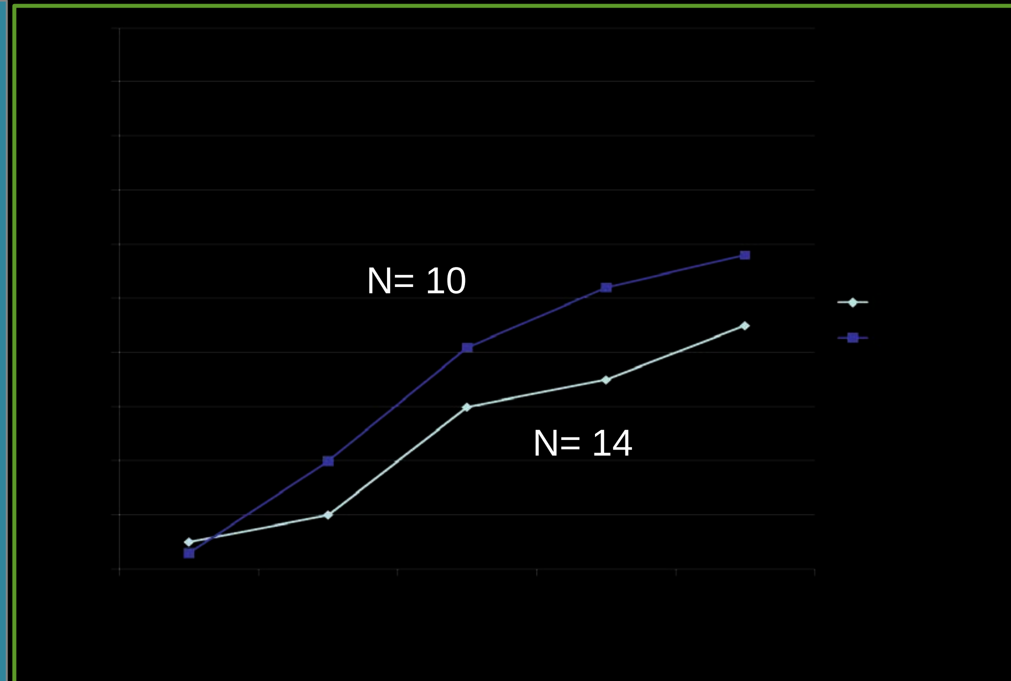
Femtolaser PK 150 KHz

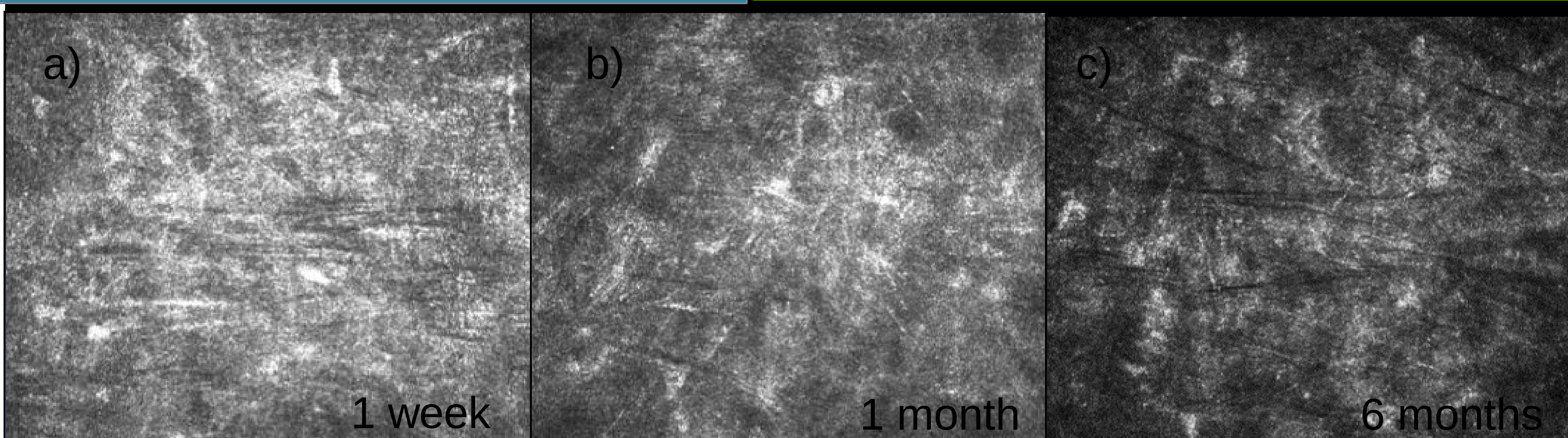


Microkeratome
DSAEK

AS-OCT assessment of cornea and PLD thickness And BCVA over time after ultra-thin FSL DSEK







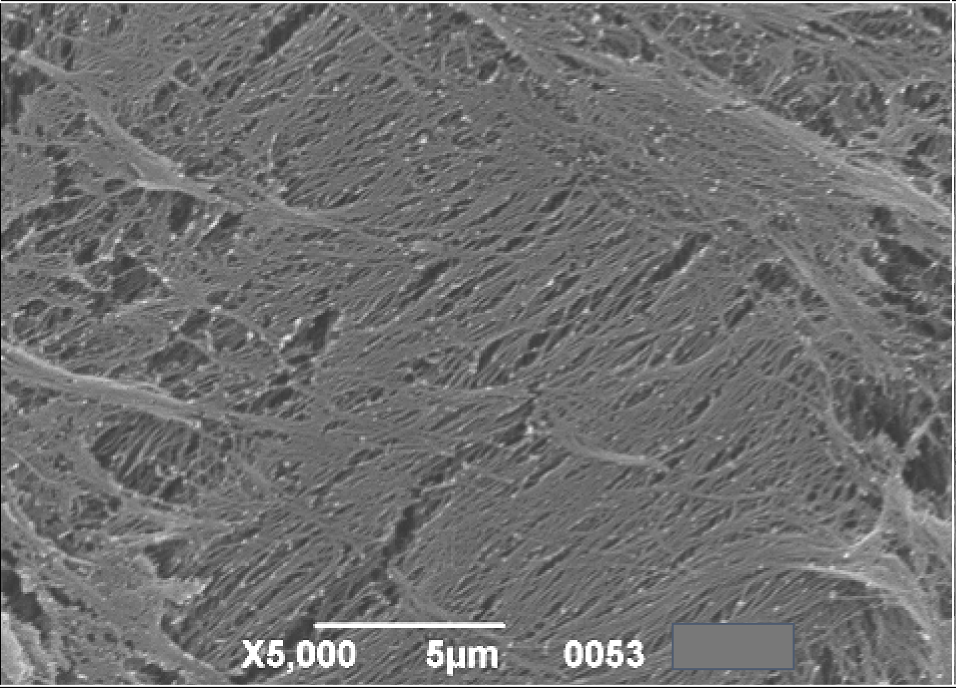
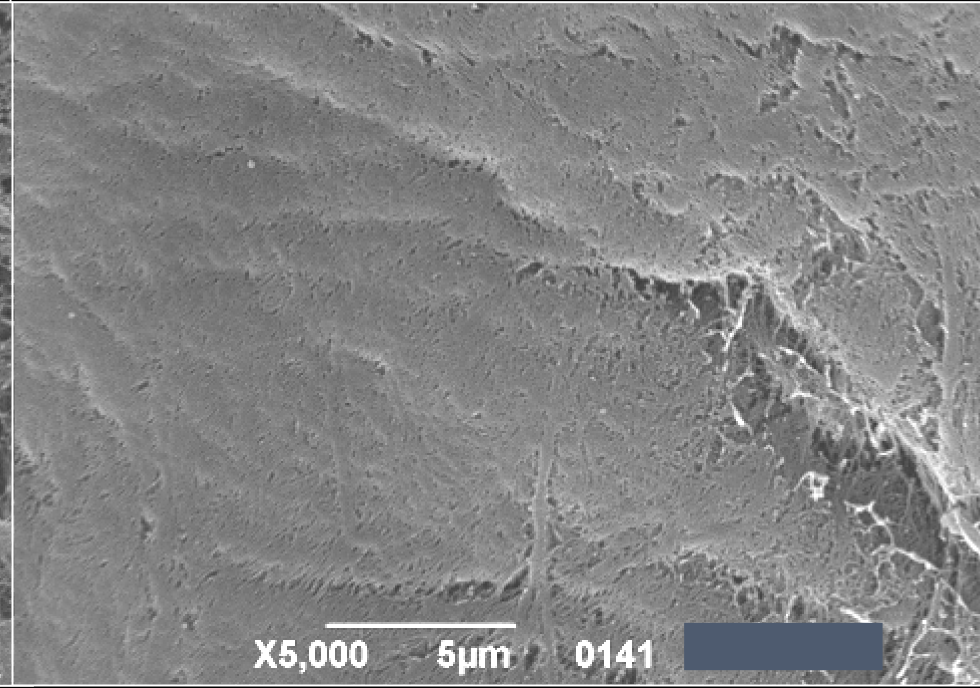
CONCLUSIONS

1. The standardized de-swelling procedure has allowed us to minimize variability of precut tissue central thickness.

2. A relatively thin graft (160 ± 30 µm) at the time of keratoplasty may offer better handling characteristics with less manipulation and faster apposition to the host cornea.

3. Larger and longer-term studies may be required to evaluate how graft thickness may influence the outcome and complications in DSAEK surgery

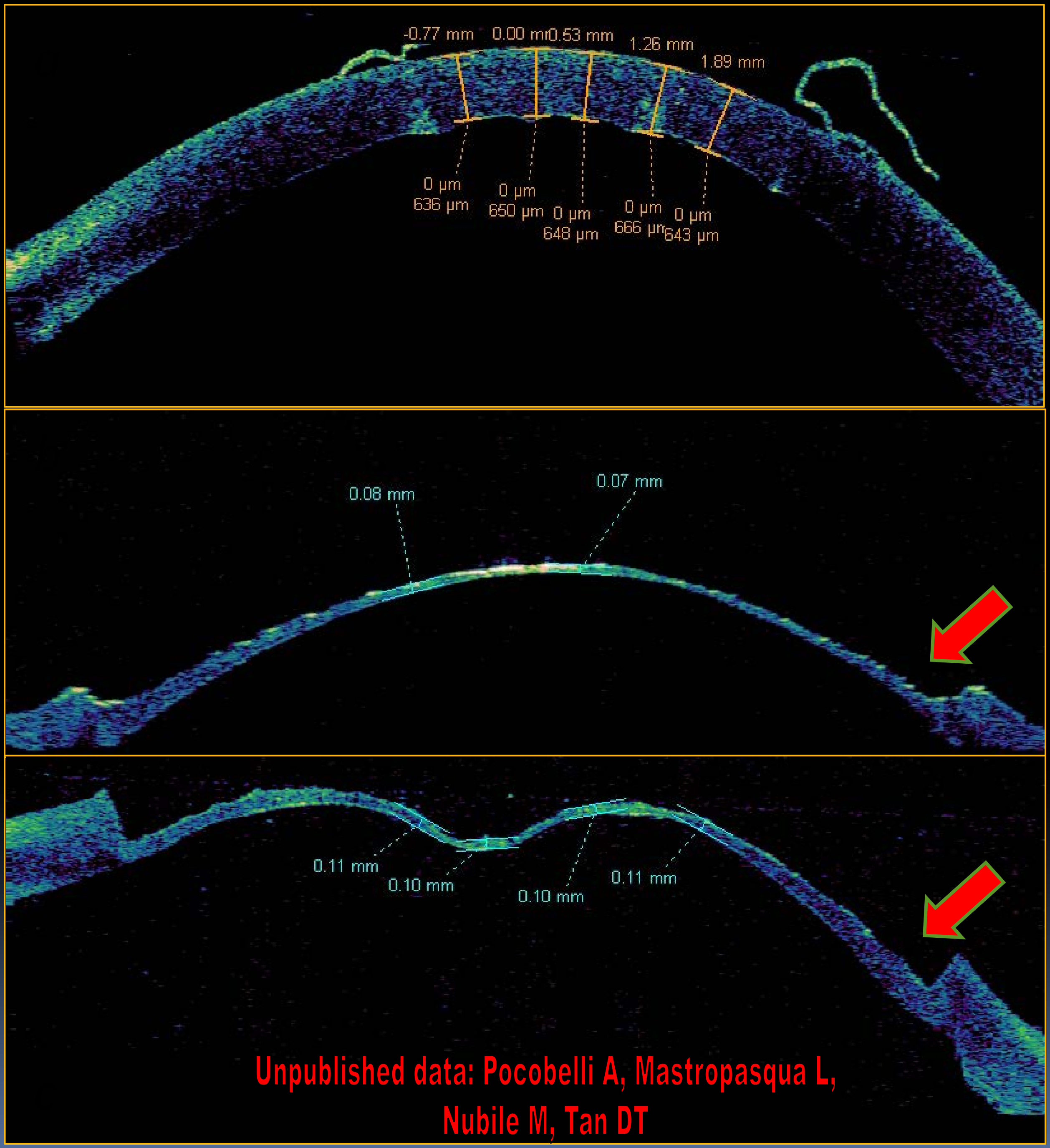
SEM picture of human corneal interface after the fs laser cut

Low laser energy	High laser energy
	

Pictures were kindly provided by

AL.CHI.MI.A.S.R.L. and Dr. M. Rossi, Ophthalmology Department, Busto Arsizio Hospital, Italy

ALCHIMIA



Unpublished data: Pocobelli A, Mastropasqua L, Nubile M, Tan DT

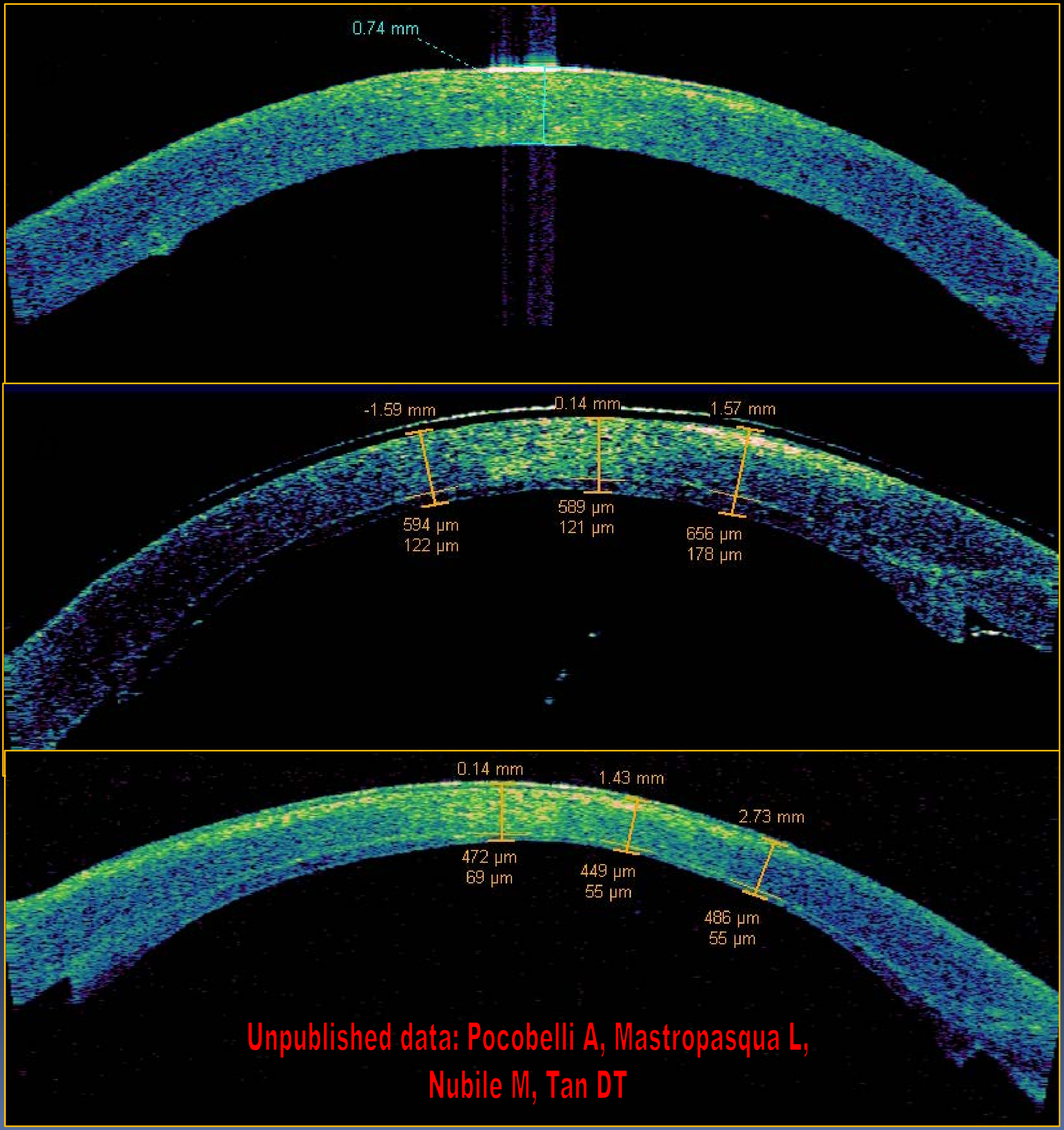
Ultra-thin FSL - DSEK

a) AS-OCT average pachymetry of donor cornea:
650 microns

b) AS-OCT pachymetry Of posterior residual stroma after: 550 microns FSL dissection
75 microns in AC

c) AS-OCT pachymetry Of posterior residual stroma after: 550 microns FSL dissection
100 microns free

Ultra-thin FSL - DSEK



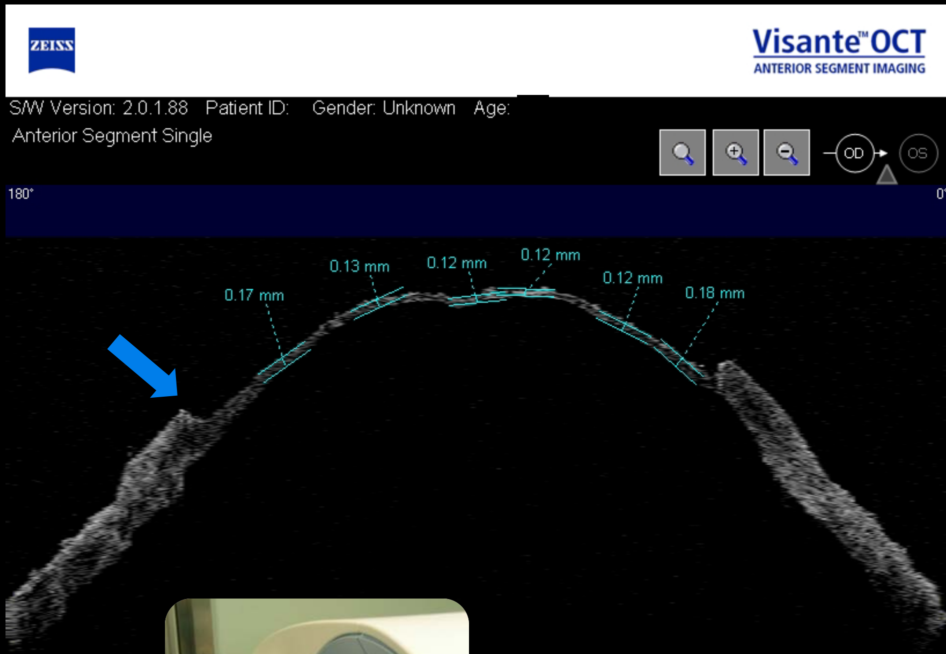
a) AS-OCT average pachymetry of preop cornea: 740 microns

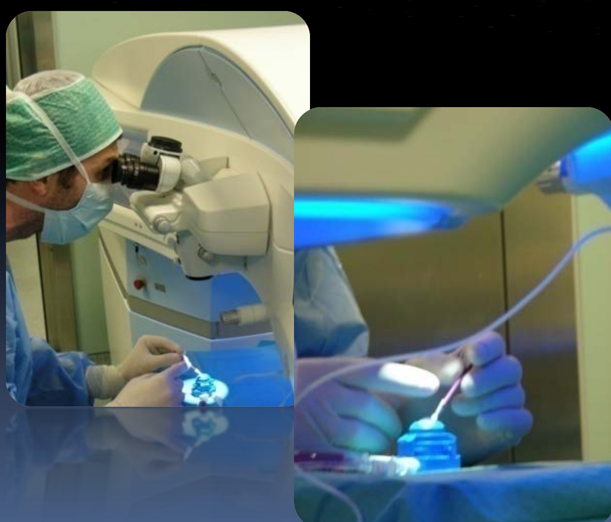
b) AS-OCT pachymetry Of host cornea and posterior lenticule 120 microns at 48 hours

c) AS-OCT pachymetry Of host cornea and posterior lenticule 55 microns at 2 weeks

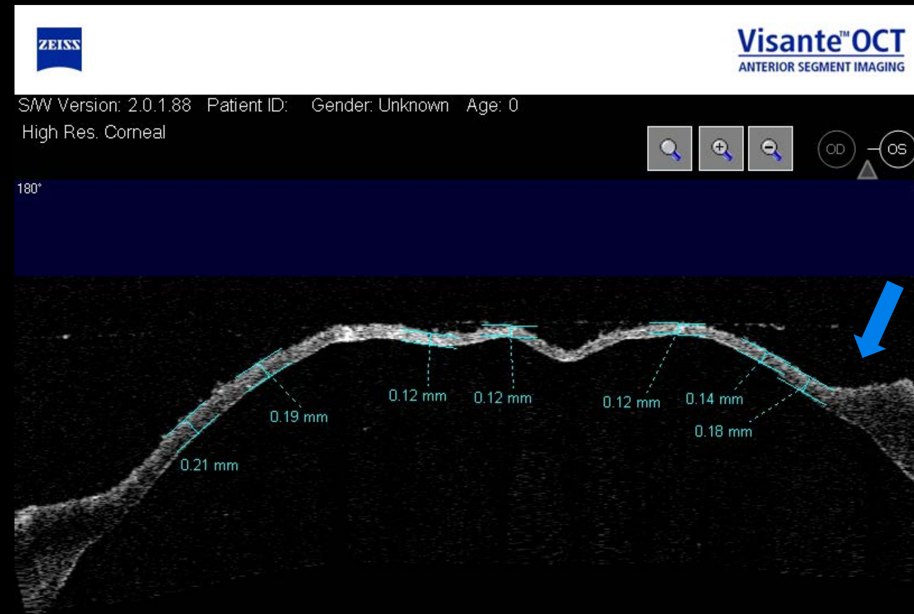
Upcoming future

Femtolaser





Microkeratome



Conclusions

- A de-swelling of the tissue before the cut allows consistent preparation of ultra-thin PLD for DSAEK with a standardized procedure
- Ultra-thin tissues can be utilized with both the Macaluso THIN-DSAEK Inserter and the Tan Endoglide without damaging the endothelium
- The Macaluso THIN-DSAEK Inserter combined with ultra-thin PLD gives the surgical advantage of a smaller incision (3.2-3.5mm)
- More corneas have to be treated to confirm the statistical significance of the present observations

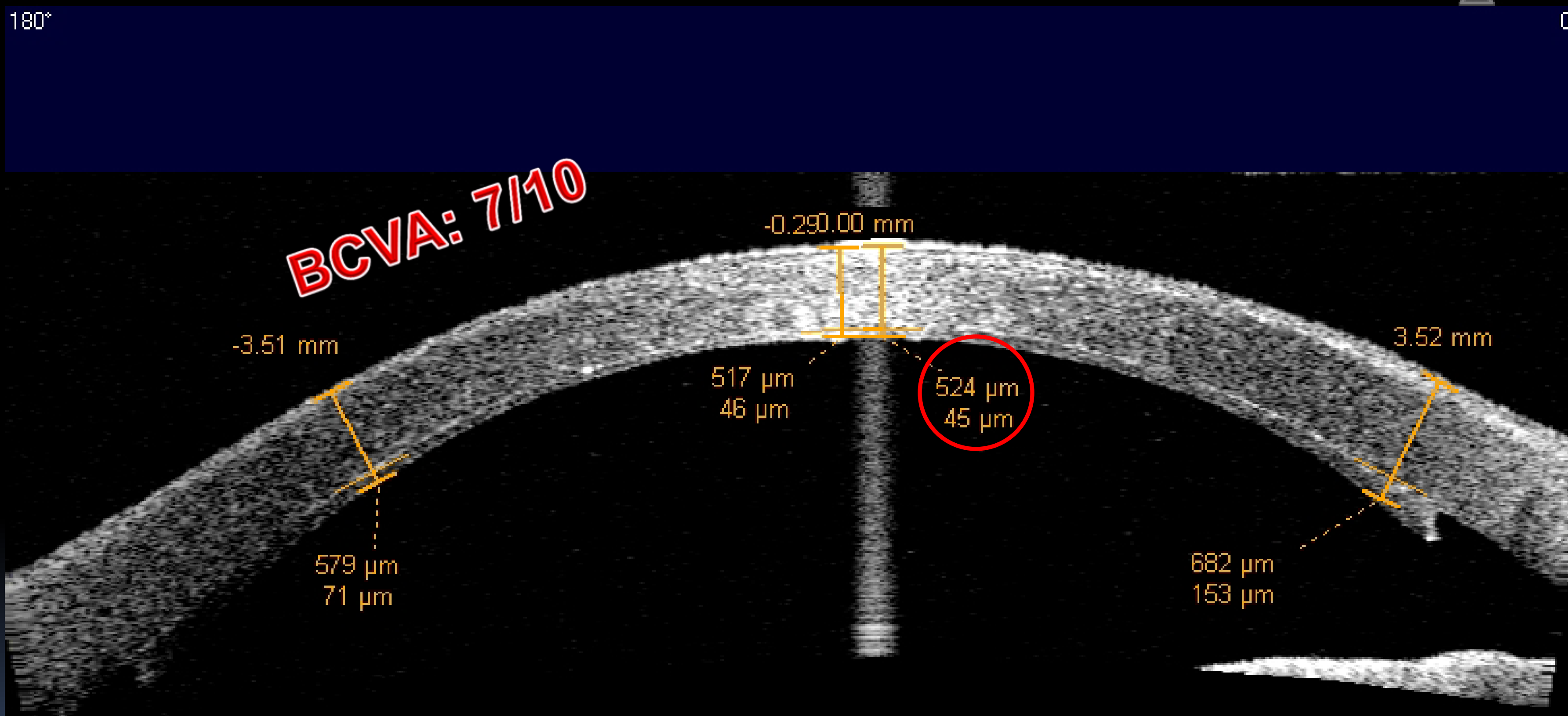
Thinner is better

7 DAYS FOLLOW-UP

Visante™ OCT
ANTERIOR SEGMENT IMAGING

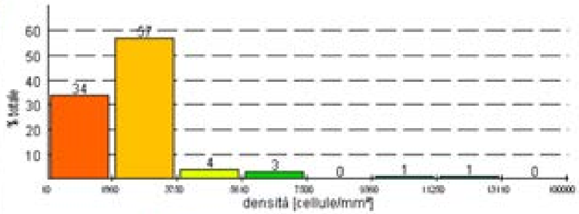
S/W Version: 2.0.1.88 Patient ID: Gender: Female Age: 85

High Res. Corneal



thin group

1 month



Conta Cellule: 2104 [cellule/mm²]

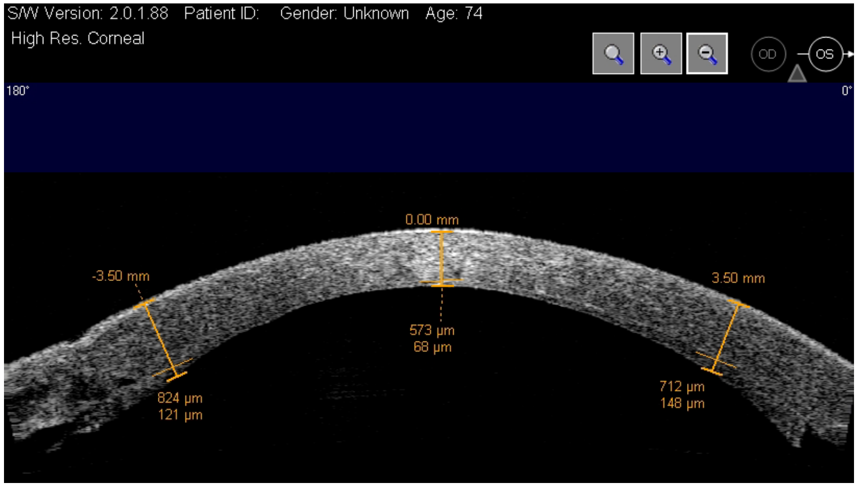
Normale: 1621 - 3145 [cellule/mm²]

Polimegatismo: 38,3 %

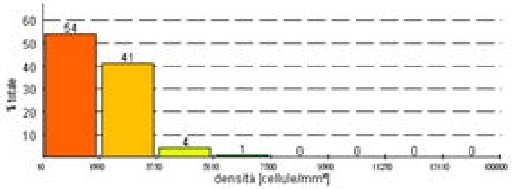
Normale: < 30 %

ZEISS

Visante™ OCT
ANTERIOR SEGMENT IMAGING



6 months



Conta Cellule: 1682 [cellule/mm²]

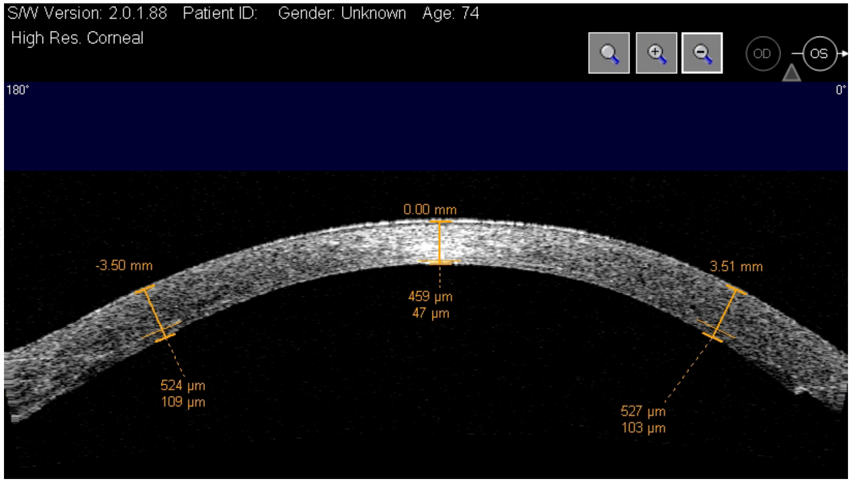
Normale: 1618 - 3141 [cellule/mm²]

Polimegatismo: 33,3 %

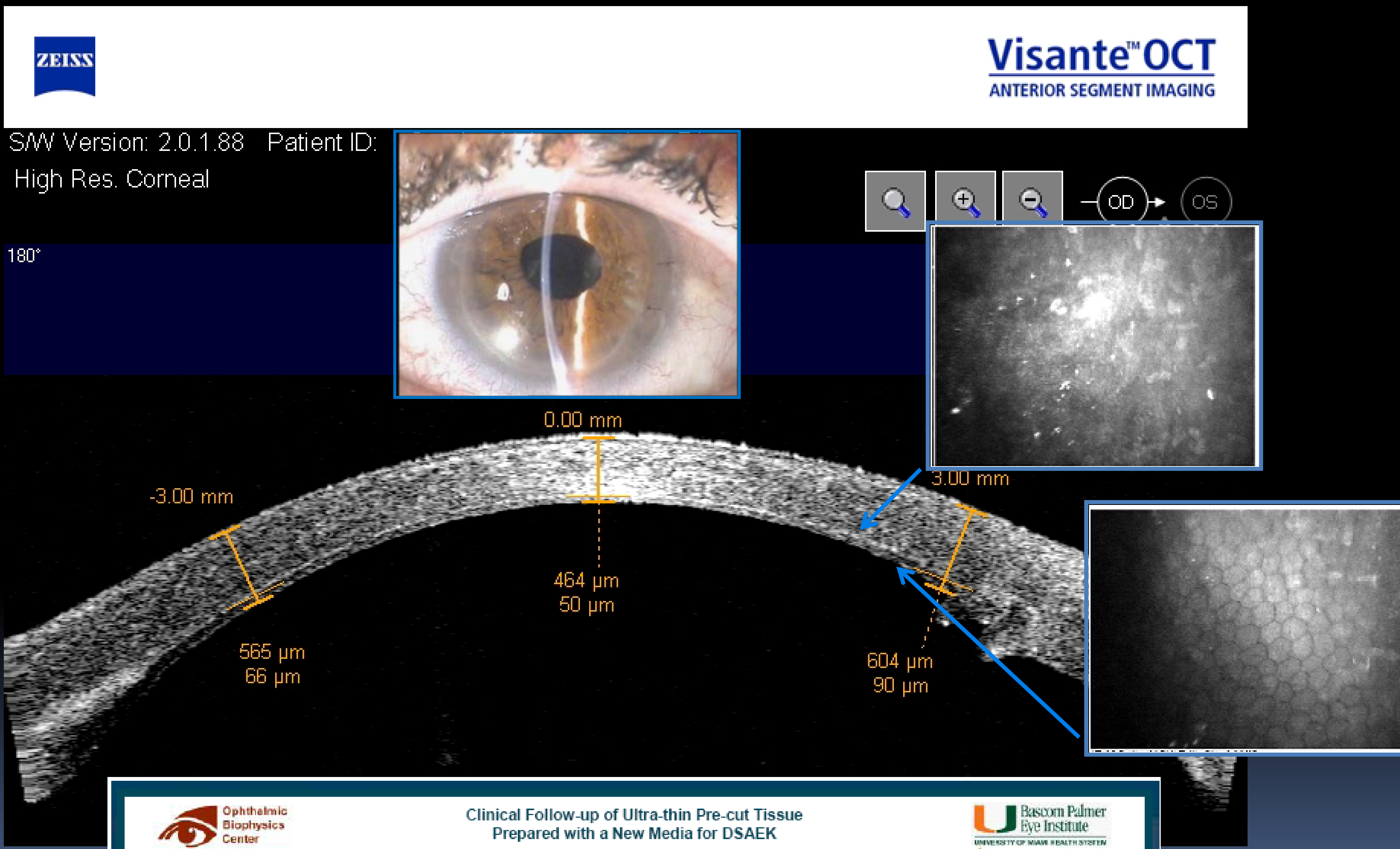
Normale: < 30 %

ZEISS

Visante™ OCT
ANTERIOR SEGMENT IMAGING



1 month follow-up
BCVA: 0.7 (thin group)



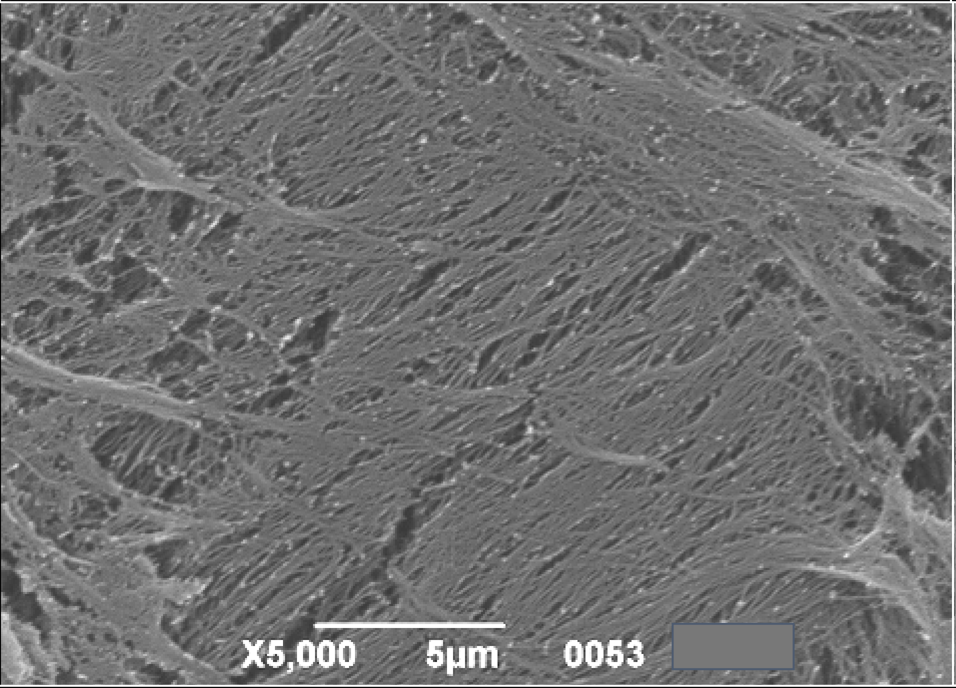
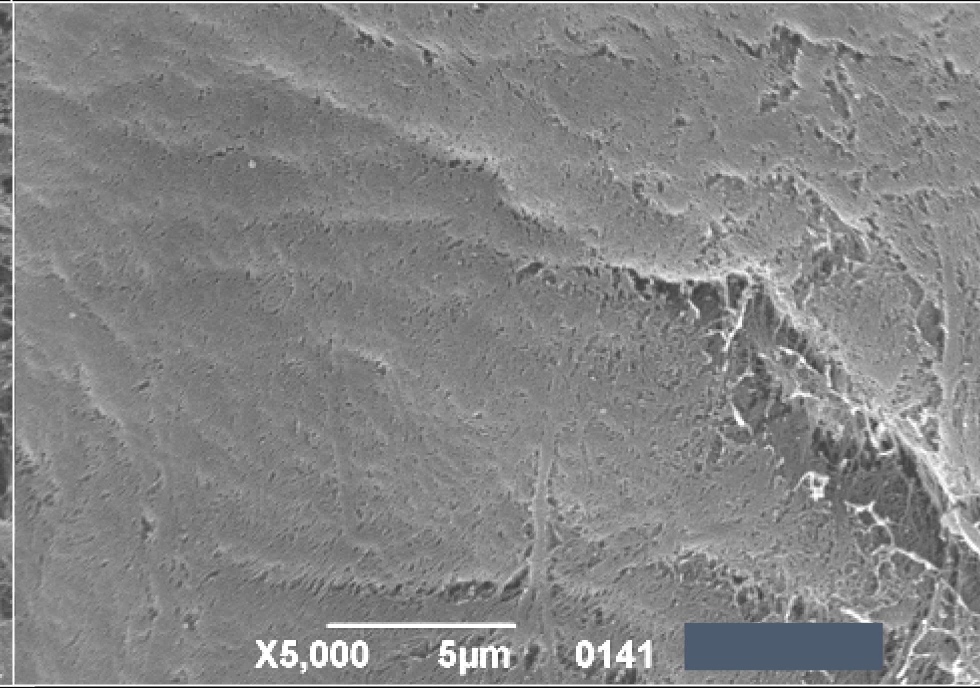
Clinical Follow-up of Ultra-thin Pre-cut Tissue Prepared with a New Media for DSAEK

Mariela Caridad Aguilar[1], Domenico Amato[2], Domenico Schiano Lomoriello[2], Maria Luisa Livani[3], Jana D.Tothova[4], Mauro Beccaro[4], Sonia Yoo[1], Jean-Marie Parel[1], Augusto Pocobelli[3]

[1]Department of Ophthalmology, Ophthalmic Biophysics Center, Bascom Palmer Eye Institute, University of Miami Miller School of Medicine, Miami, Florida, USA [2]G. B. Bietti Eye Foundation IRCCS, Rome, Italy [3]S. Giovanni-Addolorata-Britannico Hospital, Rome, Italy [4]Al.Chi.M.A, SRL, Padova, Italy

Ophthalmic Biophysics Center
ALCHIMIA
Bascom Palmer Eye Institute
UNIVERSITY OF MIAMI HEALTH SYSTEM

SEM pictures of human corneal interface after the fs laser 150 KHz cut

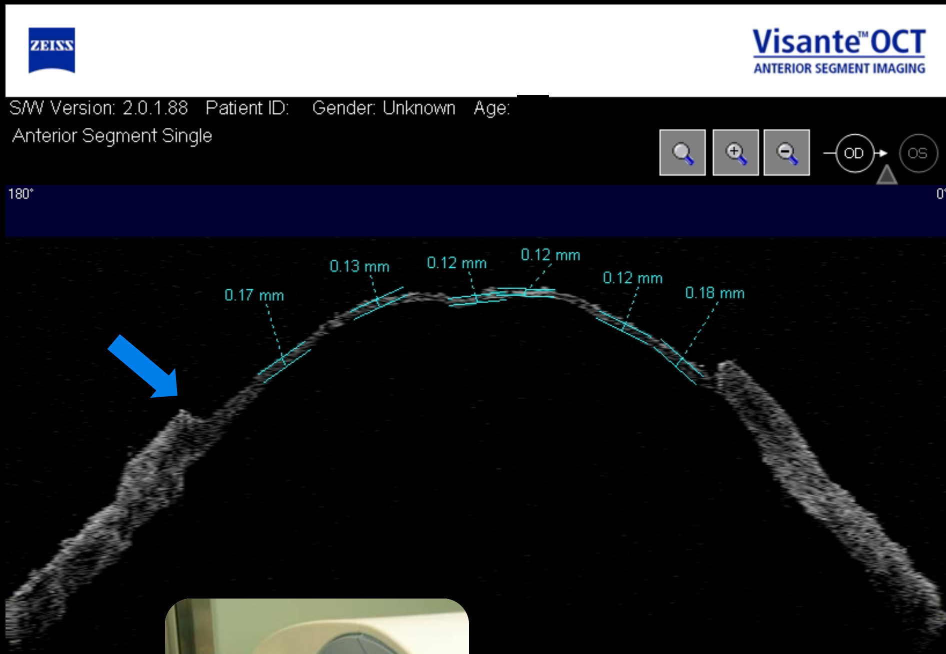
Low laser energy	High laser energy
	

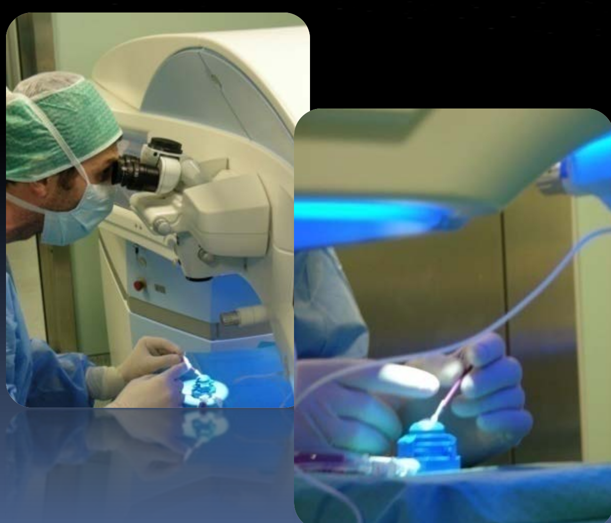
Pictures were kindly provided by

ALCHIMIA S.R.L. and Dr. M. Rossi, Ophthalmology Department, Busto Arsizio Hospital, Italy

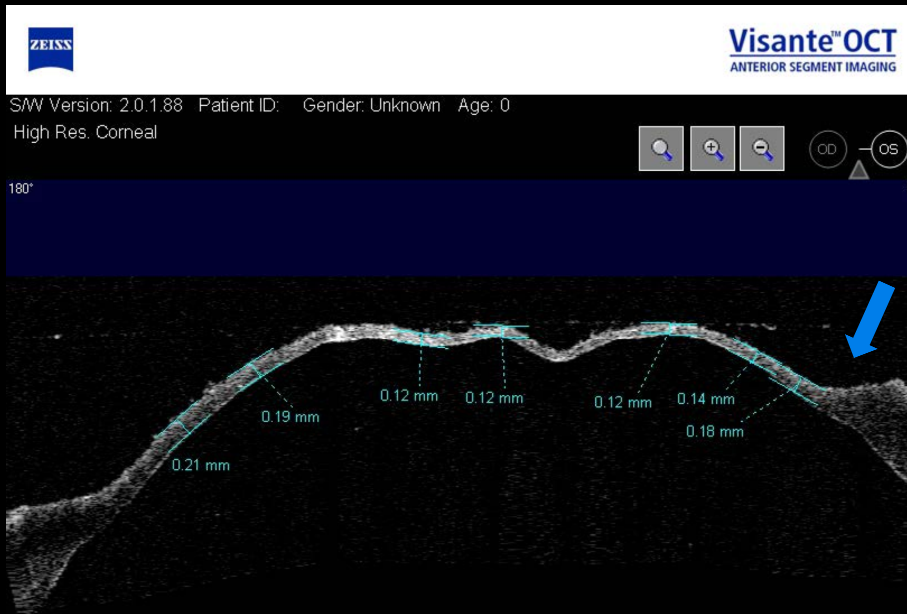
Upcoming future

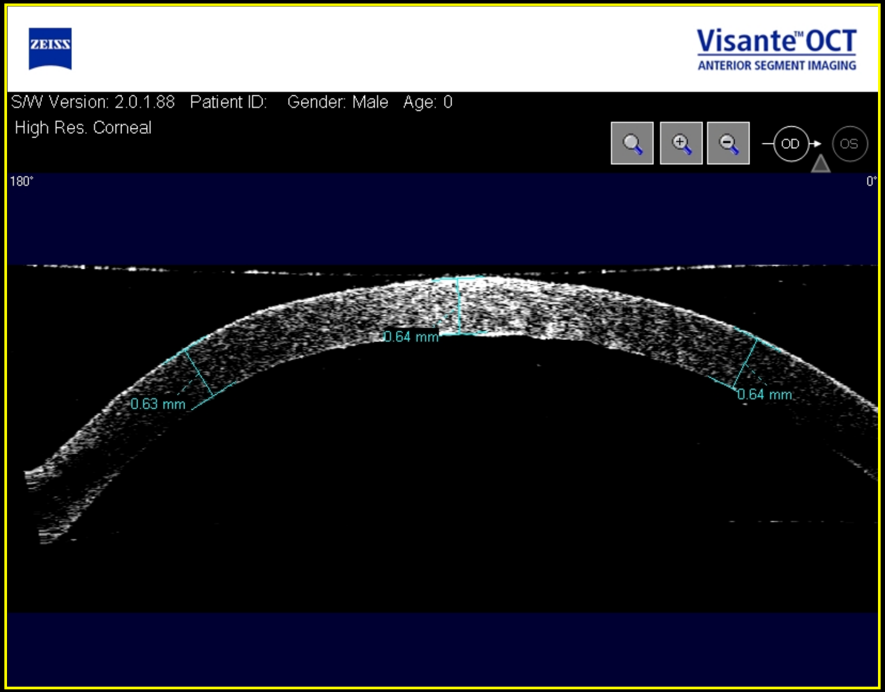
Femtolaser

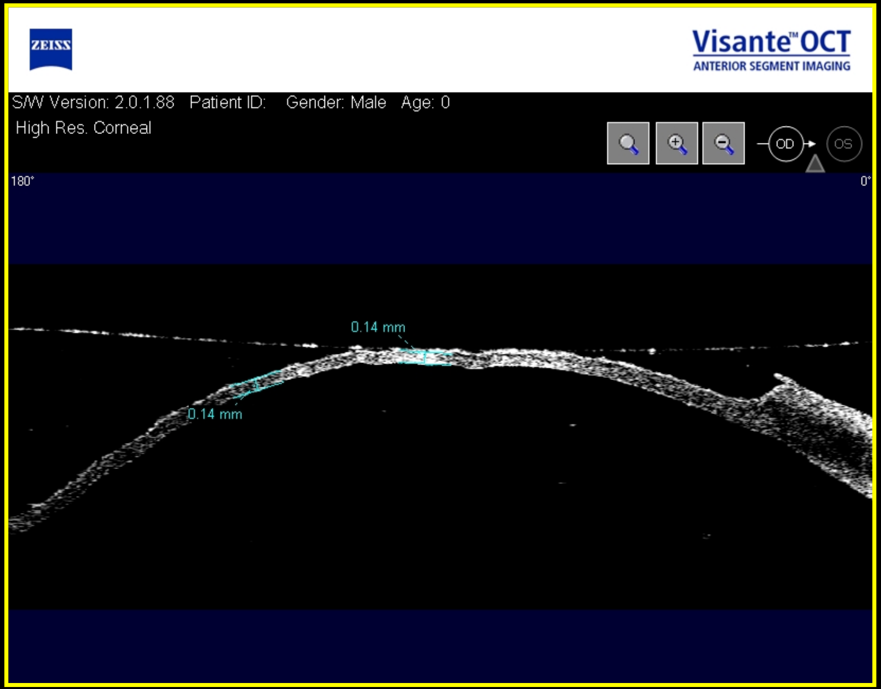


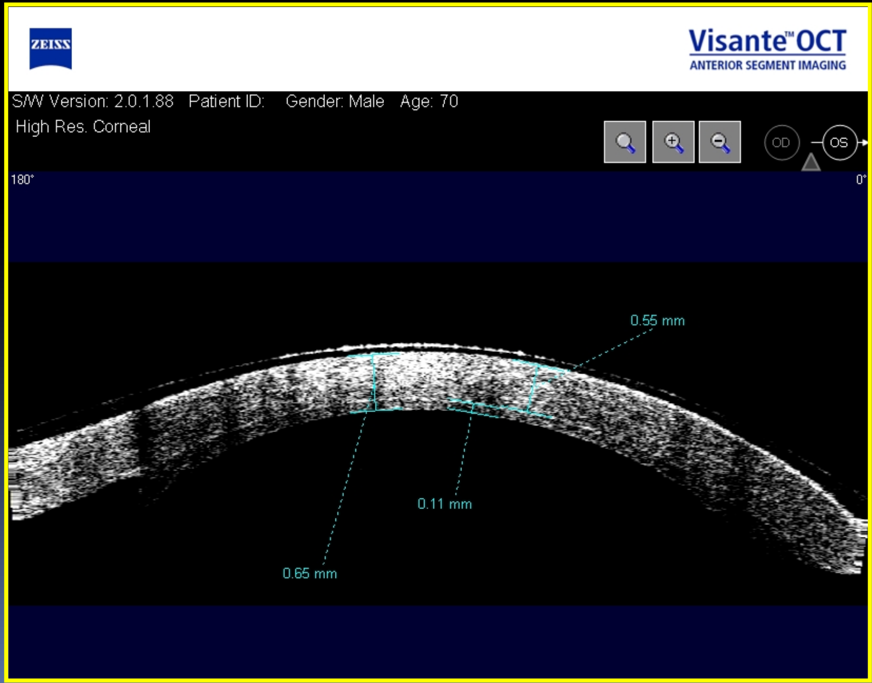


Microkeratome




Visante™ OCT
ANTERIOR SEGMENT IMAGING
S/W Version: 2.0.1.88 Patient ID: Gender: Male Age: 0
High Res. Corneal
OD
OS
180°
0°
0.64 mm
0.63 mm
0.64 mm


Visante™ OCT
ANTERIOR SEGMENT IMAGING
S/W Version: 2.0.1.88 Patient ID: Gender: Male Age: 0
High Res. Corneal
OD
OS
180°
0°
0.14 mm
0.14 mm

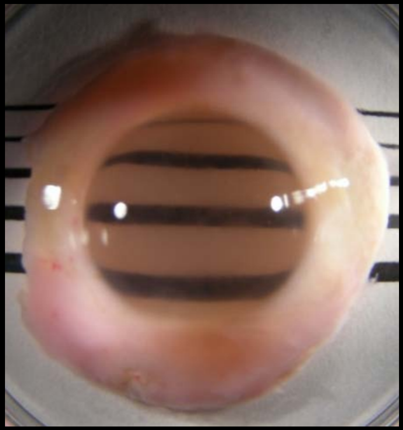

Visante™ OCT
ANTERIOR SEGMENT IMAGING
S/W Version: 2.0.1.88 Patient ID: Gender: Male Age: 70
High Res. Corneal
OD
OS
180°
0°
0.55 mm
0.11 mm
0.65 mm

Is it possible to reduce the donor corneal thickness before the microkeratome cut ?

Eusol-C
after 5 days at 4°C

Thin-C
after 4 hours at 4°C

Thin-C
after 24 hours at 4°C



Thin-C ™
(AL.CHI.MI.A. Srl)
Proprietary blend
of High and Low M.W. dextrans

For tissues stored at 4°C
with an intact epithelium

Tissue wastage: NONE