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Predictive factors for obtaining an ultra-thin endothelial flap: dream or reality?

Descemet's stripping automated endothelial keratoplasty (DSAEK)

•In **2023**, the Eye Bank Association of America **(EBAA)** reported a total of **33,715 EK.**
Of these, 32.4% DSAEK.

•**Graft thickness** is a critical determinant of **postoperative visual acuity.**

•**Thinner grafts** are associated with **improved visual outcomes,** particularly in patients without vision-limiting comorbidities, as they **reduce graft asymmetry**, **minimize** posterior corneal **higher-order aberrations (HOAs)**, and enhance overall **visual quality.**

•Thereby, **thin (T; <130µm)** and **ultrathin (UT; <100µm)** DSAEK **(T/UT-DSAEK)** were developed to increase the **visual outcomes** of DSAEK and to maintain their **technical accessibility**.

Van Meter W, Mathews P, Philippy B, DeMatteo J. 2023 Eye Banking Statistical Report—Executive Summary. Eye Banking and Corneal Transplantation. 2024 Dec

Dickman et al, Effects of Graft Thickness and Asymmetry on Visual Gain and Aberrations After Descemet Stripping Automated Endothelial Keratoplasty. JAMA Ophthalmol. 2013

Neff KD, Biber JM, Holland EJ. Comparison of central corneal graft thickness to visual acuity outcomes in endothelial keratoplasty. Cornea. 2011

Preparation of UT-DSAEK in Eye Bank with the microkeratome

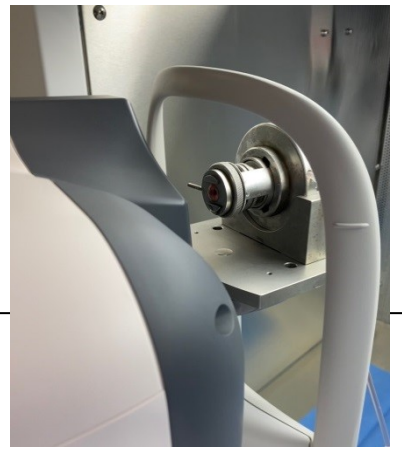
.

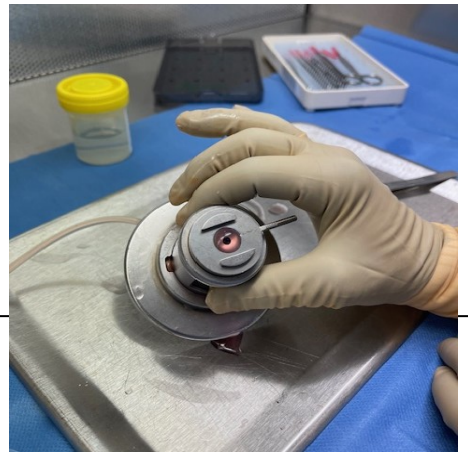
• Due to inconsistent cutting conditions, **manual microkeratome** cutting leads to **variability in graft thickness and symmetry**, reducing predictability and reproducibility.

• Recently, **mechanical microkeratome systems** have been adopted to **automate the cutting process**, ensuring consistent **artificial chamber internal pressure** and improving the reproducibility of results.

• **Microkeratome-related complications, (graft perforation or buttonholing)** in donor preparation with UT-DSAEK have been reported at **18%** ***(Sikder2011***) and **7.2%** (**Busin2013)** .

• Developing a reliable **protocol** to achieve the **desired graft thickness without perforation** is crucial for improving patient outcomes and **conserving donor corneas**, especially given the global **shortage of corneal tissue.** *(Gain2016)*





Refining Techniques to Optimize Graft Thickness

- **Pre-cut Optimization Strategies**

  - **Air-drying** or **THIN-C medium** to reduce donor corneal thickness before a single microkeratome pass. (Roberts et al., 2015), (Bucher et al. 2015)
  - **Controlled Drying Time and Pressure:** Cornea thinned at approximately 11 µm/min under controlled artificial anterior chamber pressure 198.8mmHg (Romano et al., 2017)
  - **Epithelial Removal:** Studied by *Busin et al., 2015*. No significant impact on final graft thickness.

- **Various cutting techniques** have been developed to achieve thinner DSAEK grafts

.

  - **Double-pass** method (Busin et al, 2012),
  - **Slow-pass** technique *(Vajpayee et al., 2014)*

Factors influencing Microkeratome Cutting in DSAEK

• Despite advanced microkeratome systems, **cutting outcomes** remain **variable**.

- **Donor Age:** It has been suggested that younger corneas cut thinner due to increased stromal pliability.(Holland et al., 2015)
- **Cause of Death:** Cardiac deaths associated with deeper cuts (Nishisako et al., 2022).
- **Pre-cut Tissue Thickness:** Strong predictor of post-cut thickness (Bae et al., 2018).
- **Artificial Chamber Pressure:** Higher pressure during microkeratome cutting results in thinner grafts compared to cuts performed at lower pressures. (Romano et al, 2015)
- **Cutting Speed and Hand Pressure:** Faster speeds and firmer pressure with manual microkeratome result in thinner grafts (Holland et al., 2015).
- **Translational Speed:** No significant difference in thickness between speeds (Sanchez Ventosa et al., 2021).

Nomograms:Tools to Predict Graft Thickness

- Currently, nomograms are widely used **to predict post-cut graft thickness** based on donor and procedural variables.
- Provide **guidance** in selecting the appropriate microkeratome head size to minimize variability and improve outcomes, though **they are not absolute predictors of graft thickness.**

Cheung et al., 2018

Microkeratome head (Mean cut depth, µm)	250 (310)	300 (375)	350 (464)
Intraoperative Pachymetry Values, µm	**Predicted Residual Bed Thickness, µm**		
400	90	25	−64
425	115	50	−39
450	140	75	−14
475	165	100	11
500	190	125	36
525	215	150	61
550	240	175	86

Donor Central Pachymetry, µm	Microkeratome Head, µm	Epithelium Debridement
≥600	450	+
580–600	450	−/+
540–580	400	−/+
<540	350	—

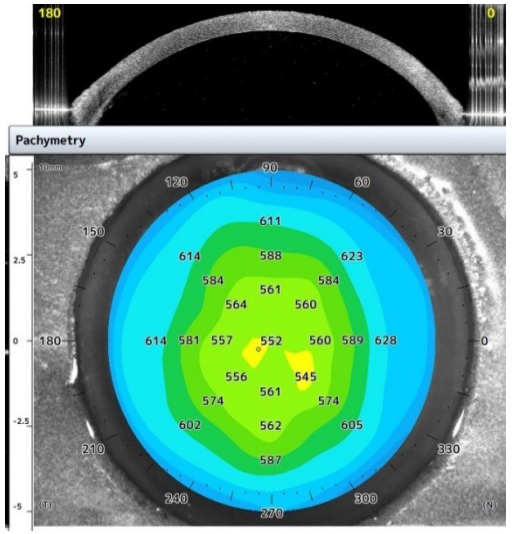
Busin et al., 2015

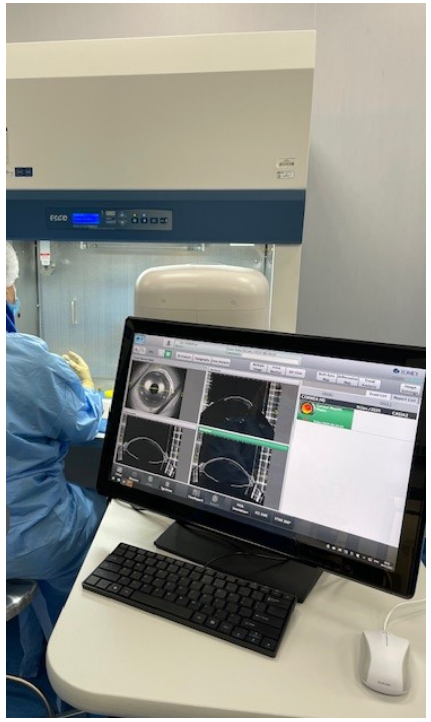
Corneal thickness (µm)	Blade head size (µm)	Eyes (n)	Precut tissue thickness (µm)		Graft thickness (µm)	
			Mean	Standard deviation	Mean	Standard deviation
510–559 (512.6–562.5)	400	12	539.58	11.54	103.50	33.46
560–610 (562.6–612.5)	450	23	591.61	13.28	97.48	29.47
610–660 (612.6–662.5)	500	13	645.31	17.80	92.31	28.37

Sánchez-Ventosa et al., 2022

METHODS

PURPOSE: To identify predictive factors of graft thickness during UT-DSAEK preparation, under standardized using a mechanical microkeratome system.





DESIGN: Single Centre Retrospective Study

SETTING: San Giovanni Addolorata Eye Bank (Rome, Italy)

STUDY POPULATION: donor eyes cut by the mechanical microkeratome system from January 2024 to December 2024.

OBSERVATION PROCEDURE: Donor- and cornea-related factors, including age, sex, cause of death, endothelial count, donor central corneal pachymetry, storage temperature, microkeratome blade size, actual cut thickness, cutting pressure, cup diameter, thickness blade gap, graft thickness, cutting thickness difference, and actual cut-to-blade ratio, were analyzed.

MAIN OUTCOME MEASURES:

Final grafts thickness was categorized into three subgroups for analysis (<70 µm; ≥70 and ≤100 µm; >100 µm).

A Multivariate linear regression was perfomed to identify pre-cut predictors of final graft thicknes

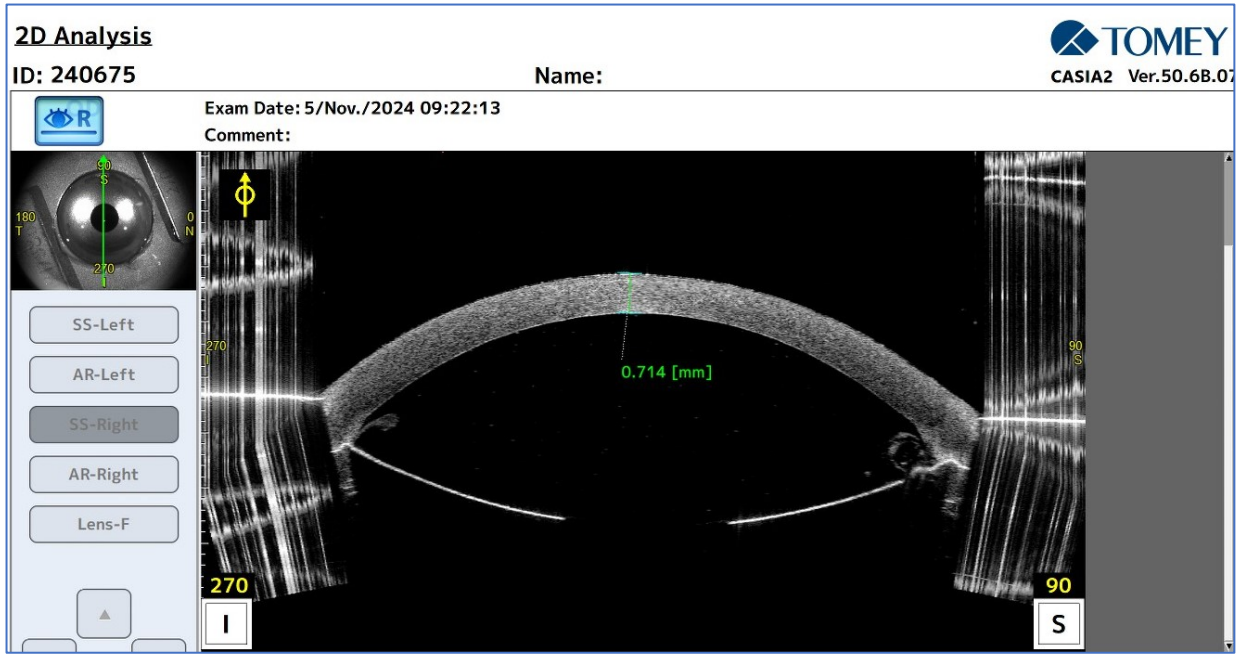
METHODS

Tissue preparation

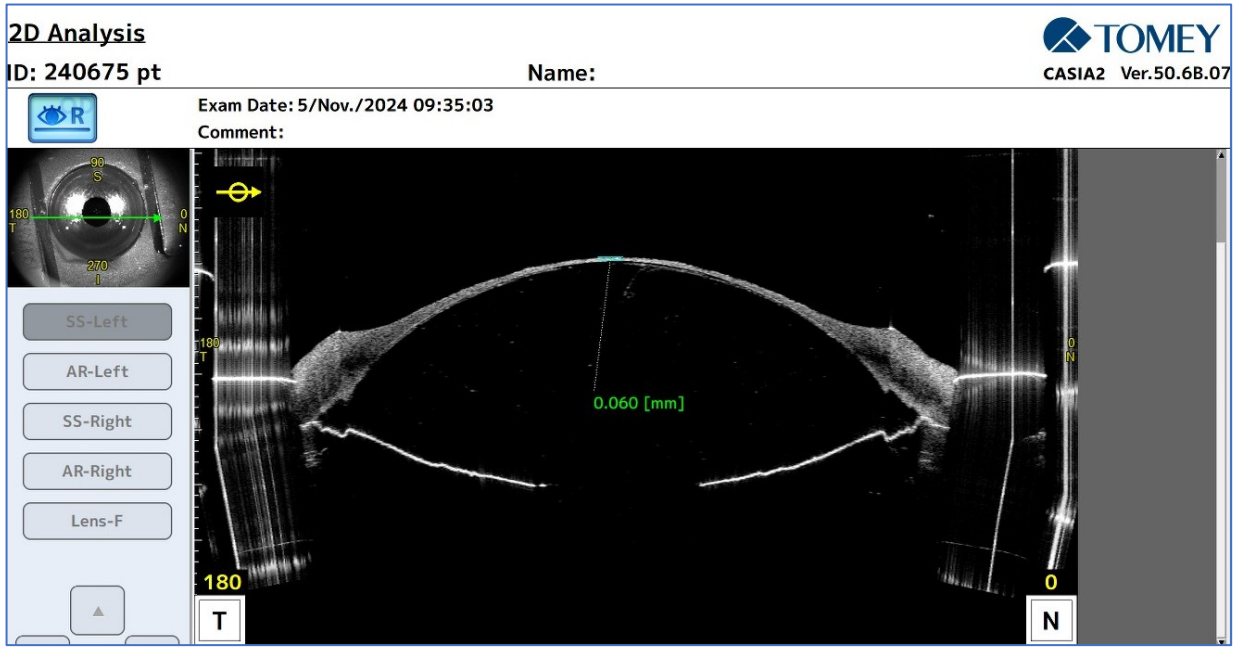
Mechanical microkeratome system using an **artificial chamber pressurizer** (ACP, Moria, Antony, France) and one use-plus automated (OUP-A, Moria).

No epithelial removal
Single pass
Speed cut of **3.0 mm/s**

Pachimetry pre cut



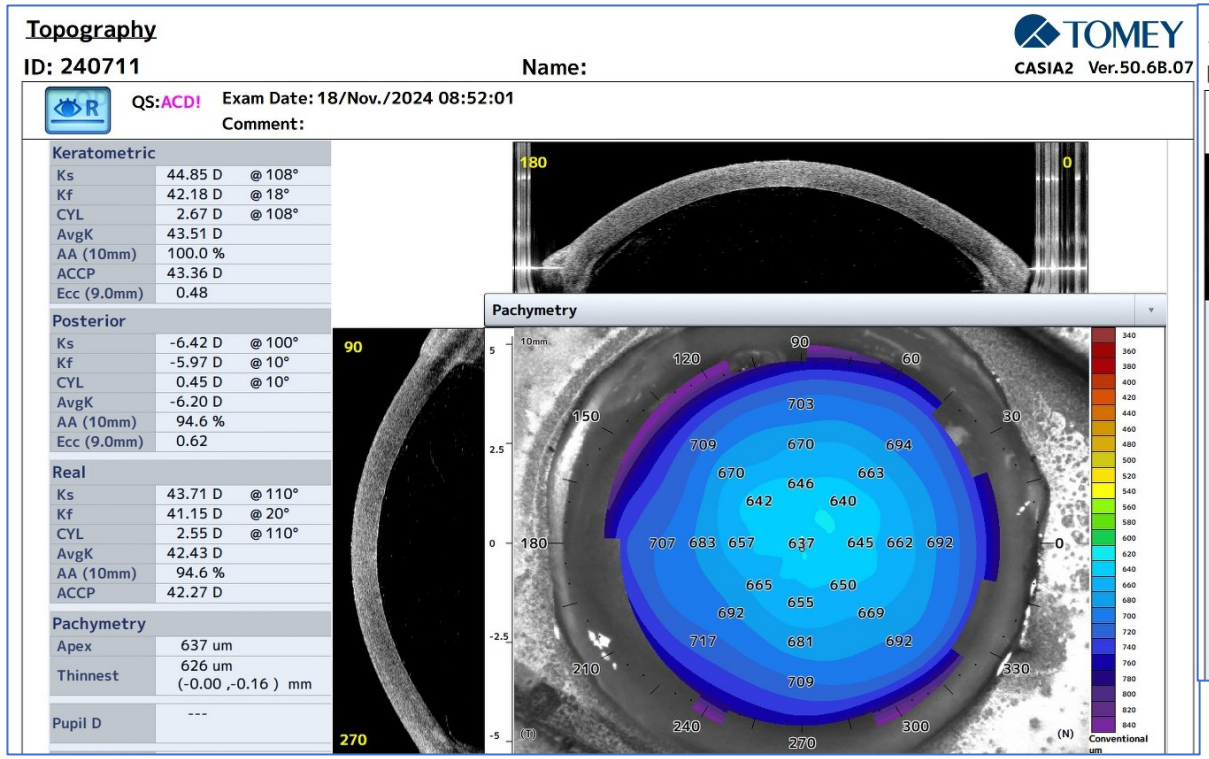
Pachimetry post cut

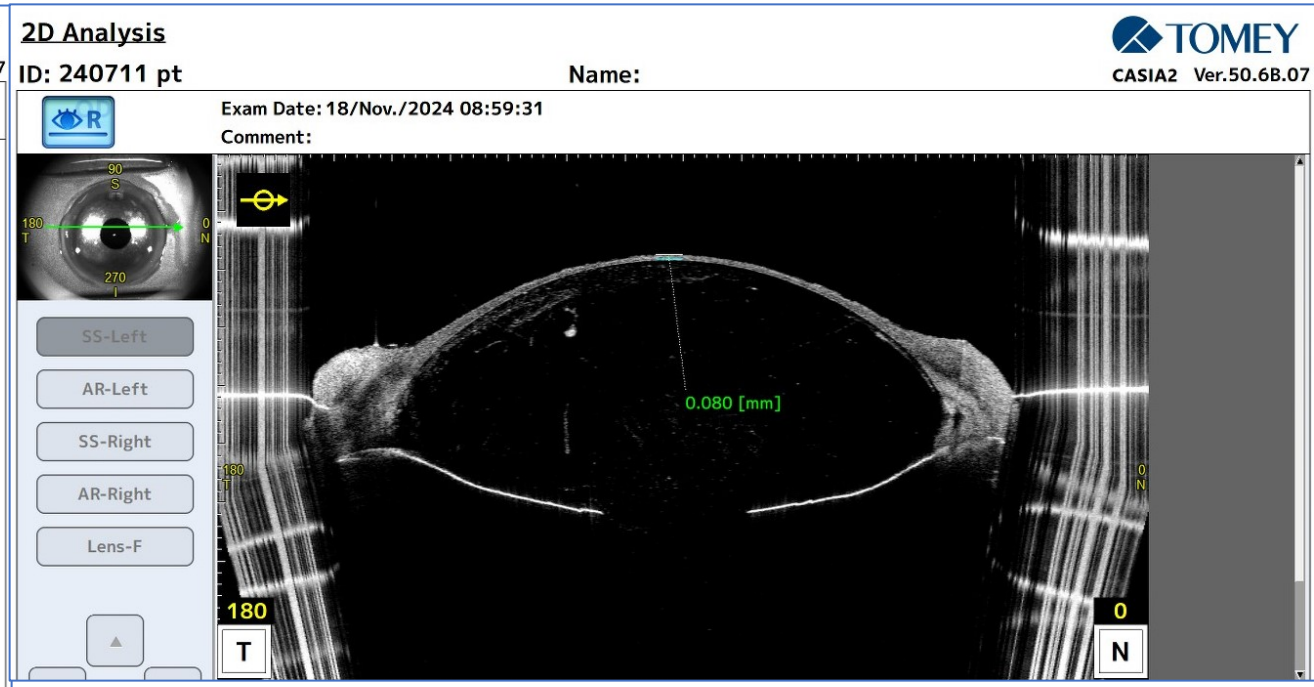


Ultra Thin tissue < 70 micron

Pachimetry pre cut

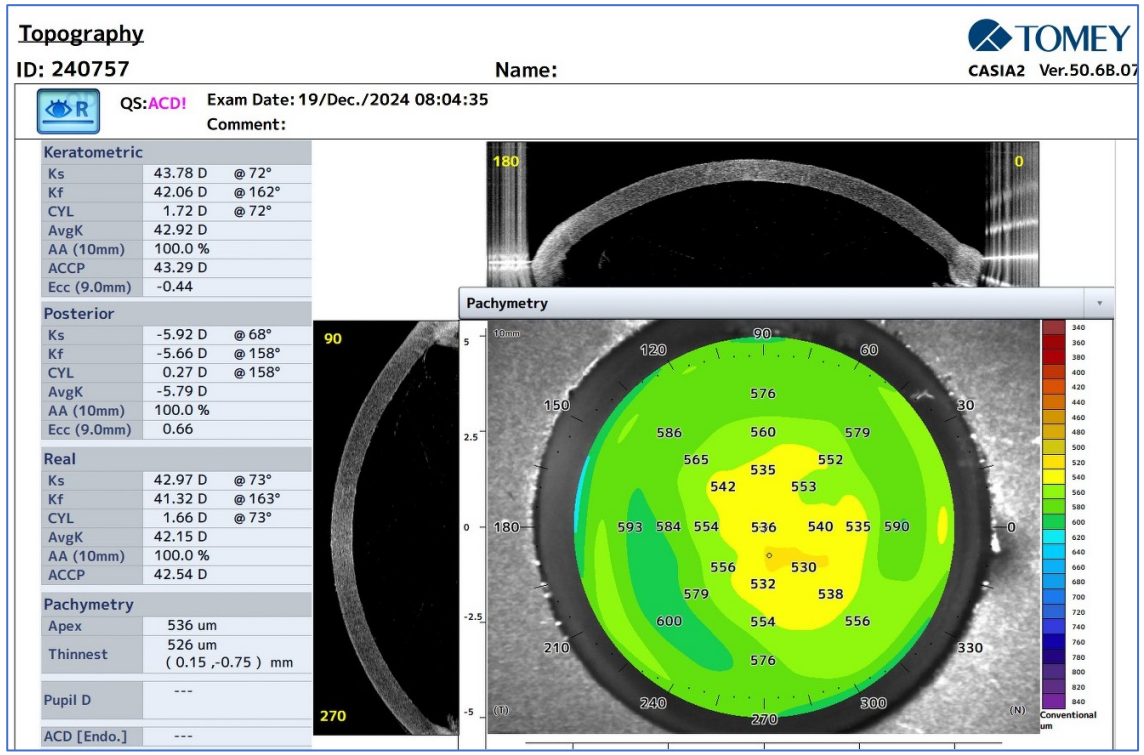
Pachimetry post cut



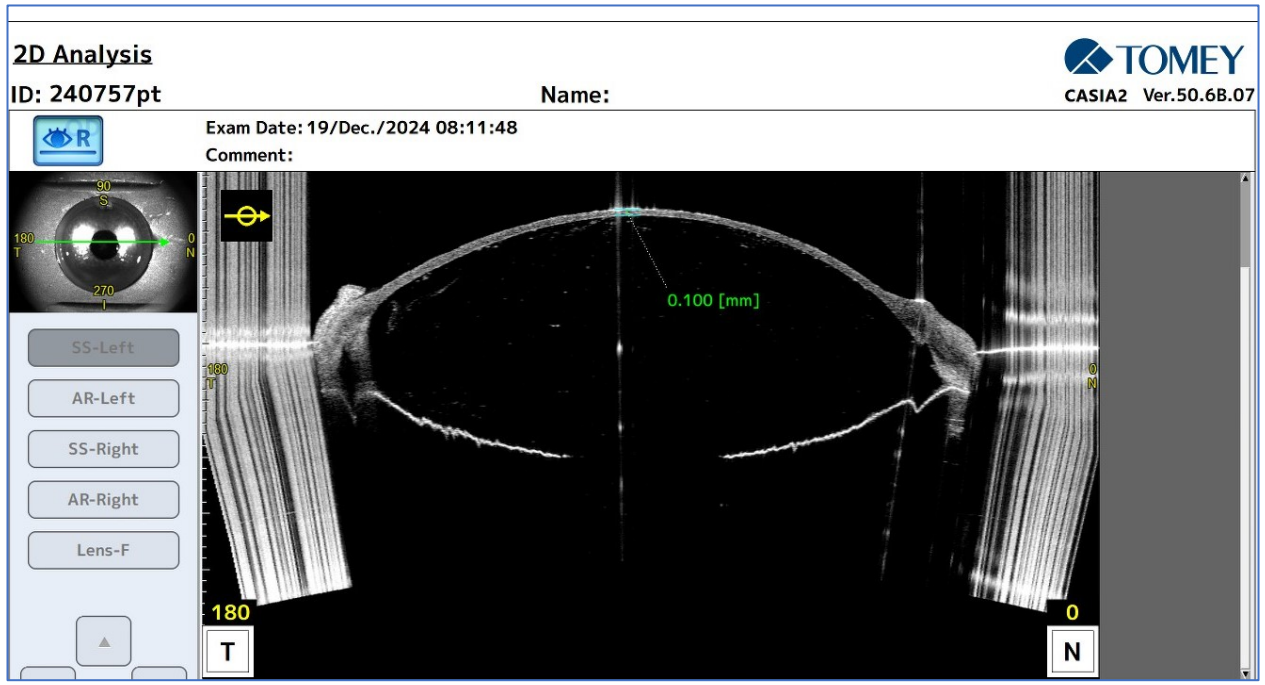


Ultra Thin tissue <100 > 70 micron

Pachimetry pre cut



Pachimetry post cut

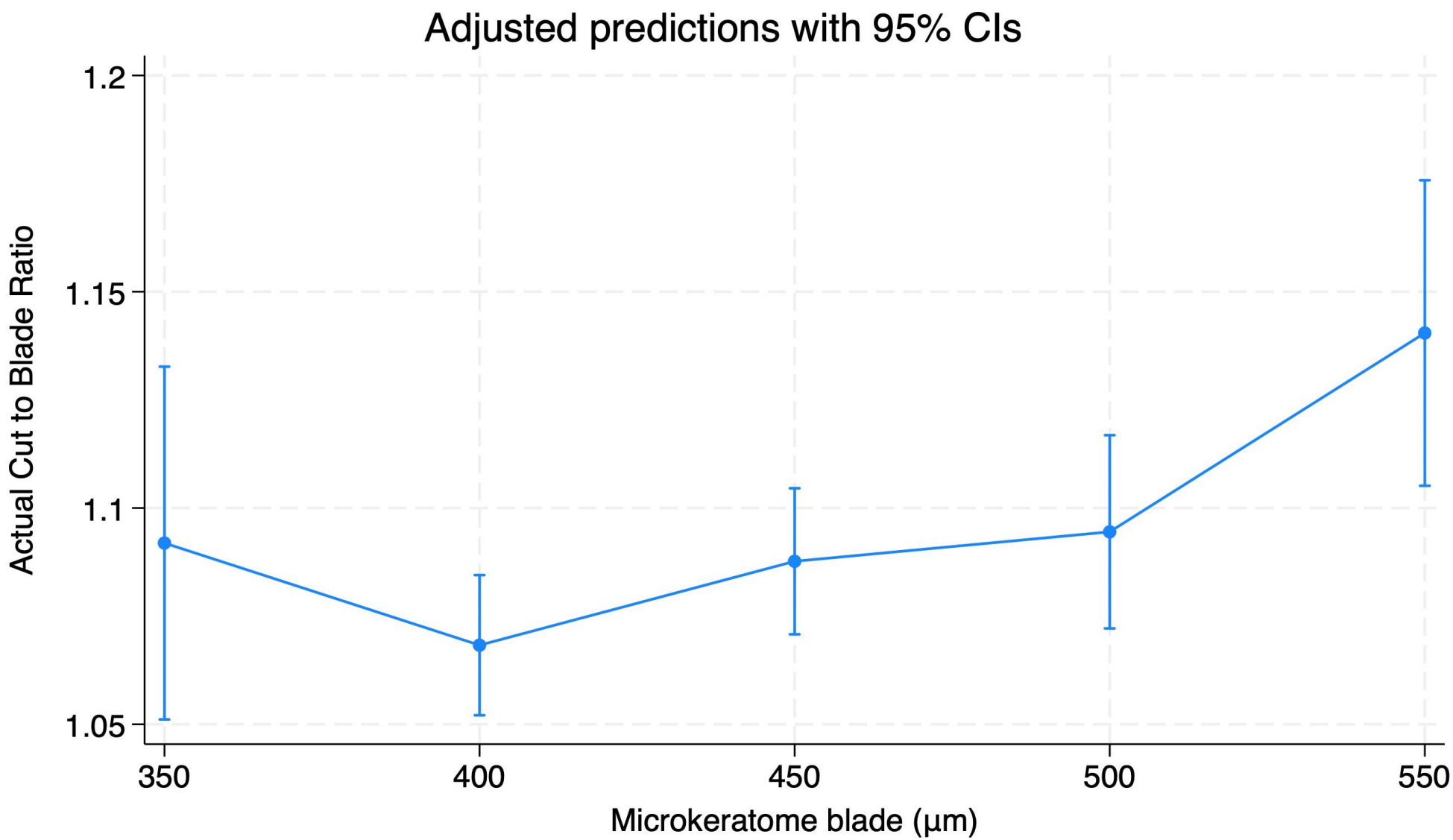


Thin tissue >100 <130 micron

RESULTS

	Total eyes (107)	Graft thickness <70µm (n. 9)	Graft thickness ≥70 and <=100µm (n. 59)	Graft thickness >100µm (n. 39)	p-value
Age, median (IQR)	63 (16)	67 (22)	63 (15)	62 (19)	0.939
Sex (female), n (%)	46 (43.0)	1 (11.1)	28 (47.5)	17 (43.6)	0.131
Cardiovascular death, n (%)	59 (55.1)	6 (66.7)	29 (49.2)	24 (61.5)	0.428
Endothelial count, mean±SD	2605±144	2589±190	2616±138	2590±143	0.623
Cold storage temperature (~4°C)	31 (29.0)	4 (44.4)	20 (33.9)	7 (17.9)	0.131
Donor central pachymetry, median (IQR)	562 (78)	590 (78)	586 (91)	552 (70)	0.162
Microkeratome, mean±SD	443.5±51.4	488.9±41.7	452.5±52.9	419.2±39.1	**<0.001**
Actual cut, mean±SD	479 (97)	560 (91)	496 (94)	441 (55)	**<0.001**
Cutting pressure, mean±SD	201.6±1.8	200.3±1.1	201.7±1.9	201.9±1.6	0.057
Cup diameter, mean±SD	10.0±0.5	10.0±0.2	10.0±0.6	9.9±0.4	0.332
Thickness blade gap, mean±SD	131.7±21.9	112.6±25.0	126.4±21.9	144.1±22.7	**<0.001**
Graft thickness, mean±SD	92.7±24.3	37.2±28.2	86.4±8.3	114.9±8.8	<0.001
Cutting thickness difference, mean±SD	39.0±25.3	75.3±28.6	40.0±22.1	29.2±21.3	<0.001
Actual Cut - Blade Ratio, mean±SD	1.08±0.05	1.15±0.05	1.09±0.05	1.07±0.05	**<0.001**

RESULTS


Adjusted predictions with 95% CIs
Actual Cut to Blade Ratio
1.2
1.15
1.1
1.05
350
400
450
500
550
Microkeratome blade (µm)

RESULTS

What factors predict final graft thickness? → Multivariate linear regression analysis of pre-cut parameters

Model Formula with Significant and Non-Significant Variables

$$\textbf{Graft thickness (µm)} = 130.71 - 0.731 \cdot \textbf{Microkeratome blade (µm)} + 0.489 \cdot \textbf{Donor central pachymetry (µm)} + \varepsilon$$

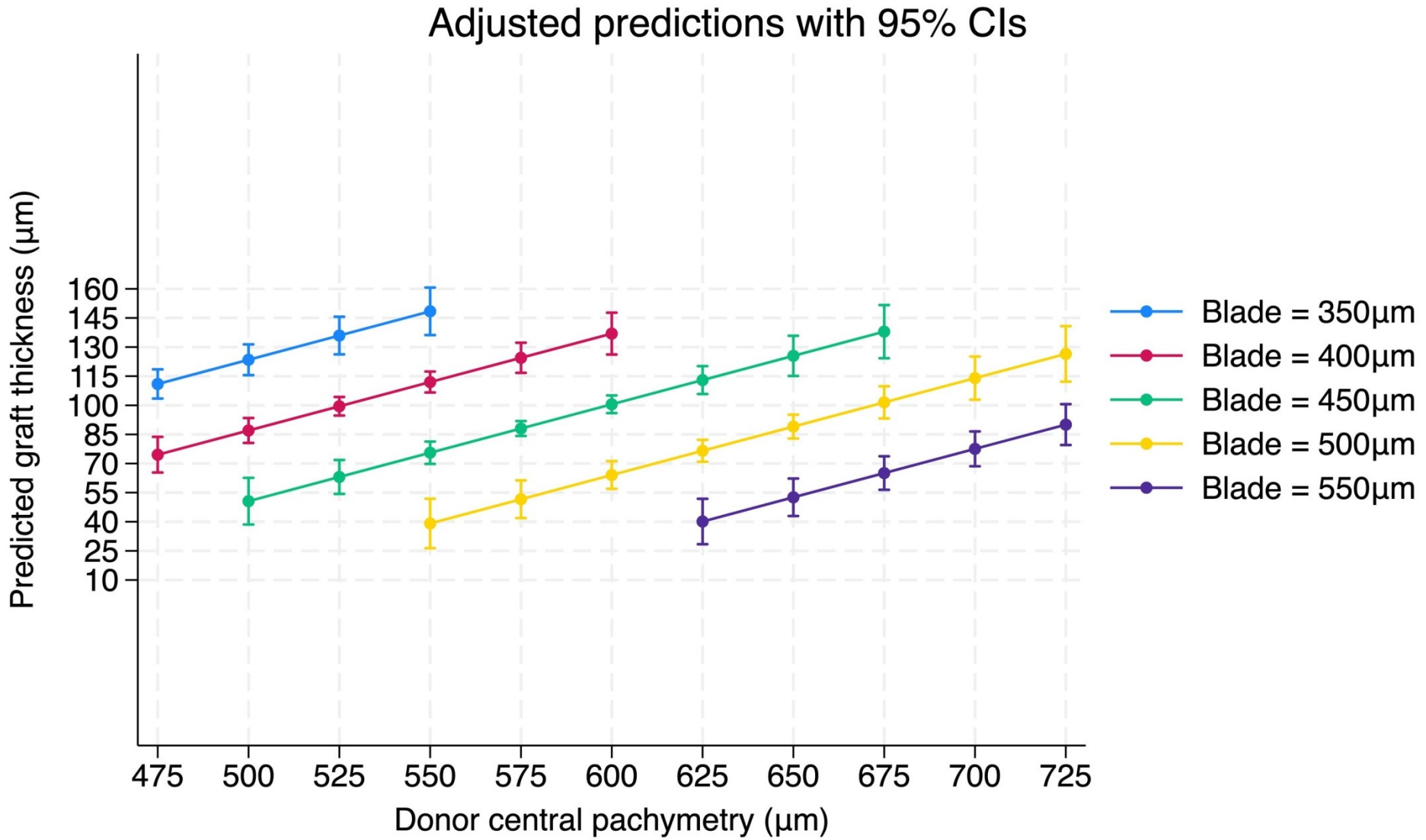
Non significant variables :

$-\textit{Female}\ (p = 0.148) :\ +5.5\ \mu m$

$-\textit{Cardiovascular death}\ (p = 0.186) :\ +5.1\ \mu m$

RESULTS

What factors predict final graft thickness? → Multivariate linear regression analysis of pre-cut parameters
→ **pseudo-R^2= 45,73%**



Limits and Considerations

- Surprisingly, no significant correlations were observed for expected parameters like donor **age** and **cutting pressure**, which was maintained relatively constant (199–207 mmHg).
- Being a **retrospective study**, it is plausible that the operator's choice of microkeratome blade was influenced by such parameters.
- **Other unconsidered factors**, such as tissue rigidity, might also influence microkeratome cutting outcomes and graft thickness.

Conclusions and Future Perpectives

• **Donor precut thickness** and **Microkeratome blade** choice and were identified as the main **predictive factors** for UT-DSAEK.

• **Prospective, blinded studies** regarding donor characteristics are needed to improve the predictive accuracy of graft preparation.

• **Analysis of new factors,** including corneal biomechanical properties such as hysteresis and stiffness, could further enhance outcome predictability and improve cutting techniques

Thank you