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**EOS 2023**



## Corneal Graft Segmental Tomography for **Rejection** Diagnosis and Prediction



Presented by

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## Financial Disclosures

- **Taher Eleiwa: None**
- **Mohamed Abou Shousha:** United States Non-Provisional Patents (Application No. 8992023 and 61809518), and PCT/US2018/013409. Patents and PCT are owned by University of Miami and licensed to Resolve Ophthalmics, LLC. This study was supported by a **NEI K23** award (K23EY026118), **NEI core center grant** to the University of Miami (P30 EY014801), and **Research to Prevent Blindness (RPB)**.



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## Introduction

- 68% of penetrating keratoplasties (PKs) are affected with at least 1 episode of rejection
- In PKs, graft failure rate secondary to rejection ranges from:
  - **5%** in low-risk grafts after five years to **35%** in high-risk grafts at three years
- Early detection is crucial to graft survival



1. Wilson SE, Kaufman HE. Graft failure after penetrating keratoplasty. *Surv Ophthalmol* 1990; 34(5): 325-356.
2. Musch DC, Schwartz AE, Fitzgerald-Shelton K, Sugar A, Meyer RF. The effect of allograft rejection after penetrating keratoplasty on central endothelial cell density. 1991; 111(6): 739-742.
3. Aلدredge OC, Krachmer JH. Clinical types of corneal transplant rejection. Their manifestations, frequency, preoperative correlates, and treatment. *Arch Ophthalmol* 1981; 99(4): 599-604.

## Tools for diagnosis



[https://upload.wikimedia.org/wikipedia/commons/thumb/b/bd/Retina\\_Group\\_slit\\_lamp\\_%28side\\_view%29.jpg/250px-Retina\\_Group\\_slit\\_lamp\\_%28side\\_view%29.jpg](https://upload.wikimedia.org/wikipedia/commons/thumb/b/bd/Retina_Group_slit_lamp_%28side_view%29.jpg/250px-Retina_Group_slit_lamp_%28side_view%29.jpg)



[https://img.medialexpo.com/images\\_me/photo-g/70682-3973457.jpg](https://img.medialexpo.com/images_me/photo-g/70682-3973457.jpg)



<https://www.nidek-intl.com/archives/004/201705/5de5d918b5788.jpg>



## Clinical diagnosis

- conjunctival injection
- Corneal edema
- Endothelial rejection lines
- Anterior chamber cells and flare
  - Exam findings present after irreversible loss of endothelial cells



6. Panda A, Vanathi M, Kumar A, Dash Y, Priya S. Corneal graft rejection. *Surv Ophthalmol.* 2007 Jul-Aug. 52 (4):375-96  
 7. Bartels MC, Doxiadis II, Colen TP et al. Long-term outcome in high-risk corneal transplantation and the influence of HLA-A and HLA-B matching. *Cornea* 2003; 22(6):552-6.

## Pachymetry



[Cornea](#). Author manuscript; available in PMC 2014 Jun 1.

PMCID: PMC3840498

Published in final edited form as:

NIHMSID: NIHMS424359

[Cornea](#). 2013 Jun; 32(6): [10.1097/ICO.0b013e31827b14c7](https://doi.org/10.1097/ICO.0b013e31827b14c7).

PMID: [23343949](https://pubmed.ncbi.nlm.nih.gov/23343949/)

doi: [10.1097/ICO.0b013e31827b14c7](https://doi.org/10.1097/ICO.0b013e31827b14c7)

### Corneal Thickness as a Predictor of Corneal Transplant Outcome

[David D. Verdier](#),<sup>1</sup> [Alan Sugar](#),<sup>2</sup> [Keith Baratz](#),<sup>3</sup> [Roy Beck](#),<sup>4</sup> [Mariya Dontchev](#),<sup>4</sup> [Steven Dunn](#),<sup>5</sup> [Robin L. Gal](#),<sup>4</sup>

[Edward J. Holland](#),<sup>6</sup> [Craig Kollman](#),<sup>4</sup> [Jonathan H. Lass](#),<sup>7</sup> [Mark J. Mannis](#),<sup>8</sup> [Jeffrey Penta](#),<sup>9</sup> and the Cornea Donor Study Investigator Group



## Specular microscopy

- Reliability
- Sampling
- Central zone



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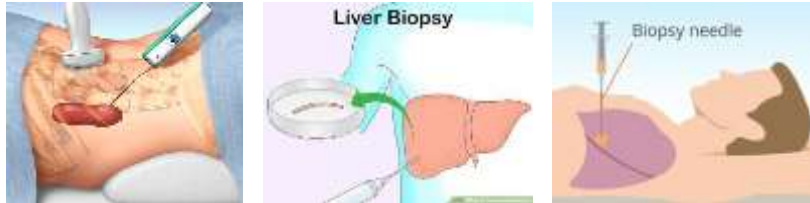


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# Solid Organ Transplantation

Rejection is diagnosed with thickening of allograft basement membranes

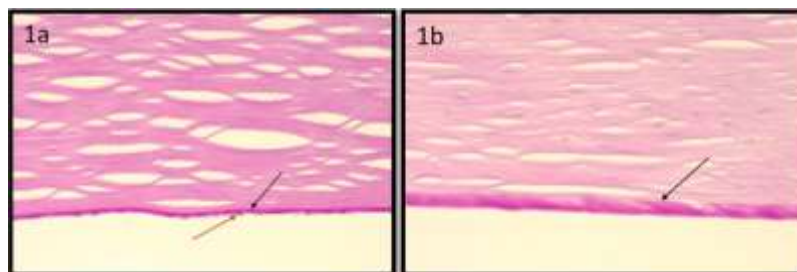


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Roufosse CA, Shore I, Moss J, et al. Peritubular capillary basement membrane multilayering on electron microscopy: a useful marker of early chronic antibody-mediated damage. *Transplantation*. 2012;94(3):269–274.  
 Shimizu T, Ishida H, Shirakawa H, et al. Clinicopathological analysis of transplant glomerulopathy cases. *Clin Transplant*. 2009;23(20):39–43.  
 Taddesse-Heath L, Kovi J. Electron microscopic findings in hepatic allograft rejection. *J Natl Med Assoc*. 1994;86(10):779–782.

# What about Corneal Grafts?

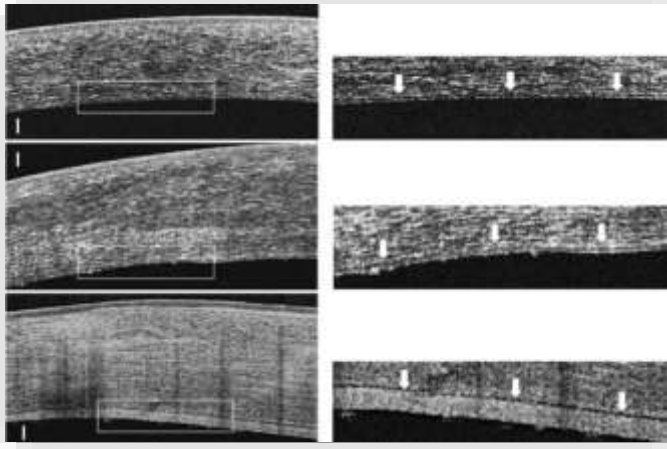
Corneal biopsies show thickening of Descemet's membrane (DM) during graft rejection



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VanDenBerg R, Diakonis VF, Bozung A, et al. Descemet Membrane Thickening as a Sign for the Diagnosis of Corneal Graft Rejection: An Ex Vivo Study. *Cornea*. 2017;36(12):1535-1537. doi:10.1097/ICO.0000000000001378

## AS-OCT features of corneal grafts



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## AS-OCT features of corneal grafts

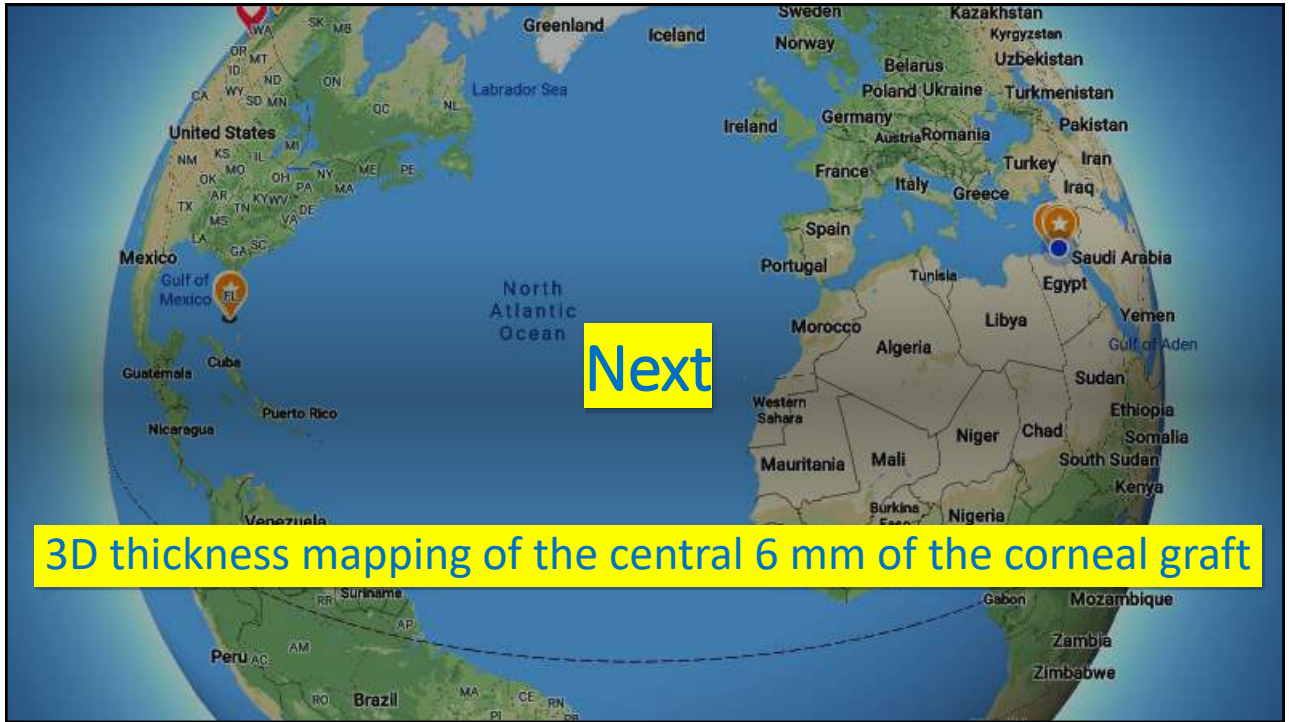
- Two-dimensional, meridional
- Central points
- Not regional
- Can miss an ongoing rejection

LIMITATION



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 **ARVO** JOURNALS

tvst

<https://doi.org/10.1167/tvst.8.3.39>

Article

## Automatic Segmentation of Corneal Microlayers on Optical Coherence Tomography Images

Amr Elsawy<sup>1,2</sup>, Mohamed Abdel-Mottaleb<sup>2</sup>, Ibrahim-Osama Sayed<sup>1</sup>, Dan Wen<sup>1</sup>,  
Vatookarn Roongpoovapatr<sup>1</sup>, Taher Eleiwa<sup>1,3</sup>, Ahmed M. Sayed<sup>1,4</sup>, Mariam Raheem<sup>1</sup>,  
Gustavo Gameiro<sup>1</sup>, and Mohamed Abou Shousha<sup>1,2,5</sup>

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## Healthy corneas

Current Eye Research >  
Volume 45, 2020 - Issue 6

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Cornea

### In-vivo Three-dimensional Characteristics of Bowman's Layer and Endothelium/Descemet's Complex Using Corneal Microlayer Tomography in Healthy Subjects


Taher K. Eleiwa , Amr Elsayy, Zeba A. Syed, Vatookarn Roongpoovapatr, Ahmed M. Sayed, Sonia H. Yoo & ... show all

Pages 659-667 | Received 03 Jun 2019, Accepted 26 Oct 2019, Published online: 18 Feb 2020

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## Fuchs endothelial cell dystrophy


Ophthalmology  AMERICAN ACADEMY OF OPHTHALMOLOGY®  
Protecting Sight. Empowering Lives.

Article in Press


### Diagnostic Performance of 3-Dimensional Thickness of the Endothelium–Descemet Complex in Fuchs' Endothelial Cell Corneal Dystrophy

Taher Eleiwa, MD, MSc<sup>1,2</sup>, Amr Elsayy, MSc<sup>1,2</sup>, Mohamed Tolba, MD<sup>1,4</sup>, William Feuser, MS<sup>5</sup>, Sonia Yoo, MD<sup>3</sup>, Mohamed Abou Shousha, MD, PhD<sup>1,2,4</sup>  

Manuscript no. D-19-00018.

 PilotX Metrics

DOI: <https://doi.org/10.1016/j.ophtha.2020.01.021>

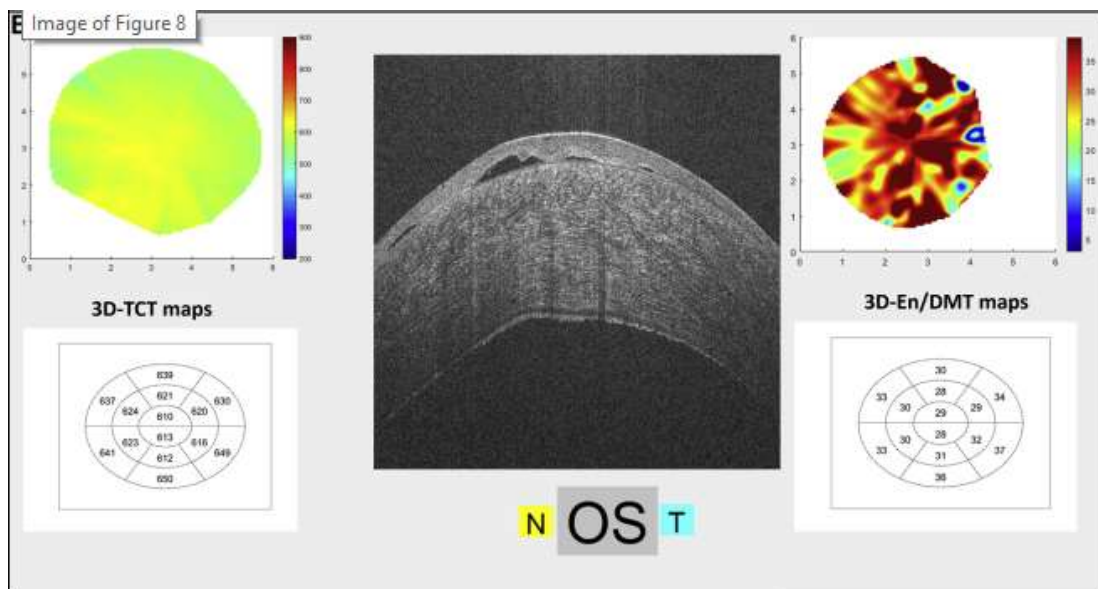
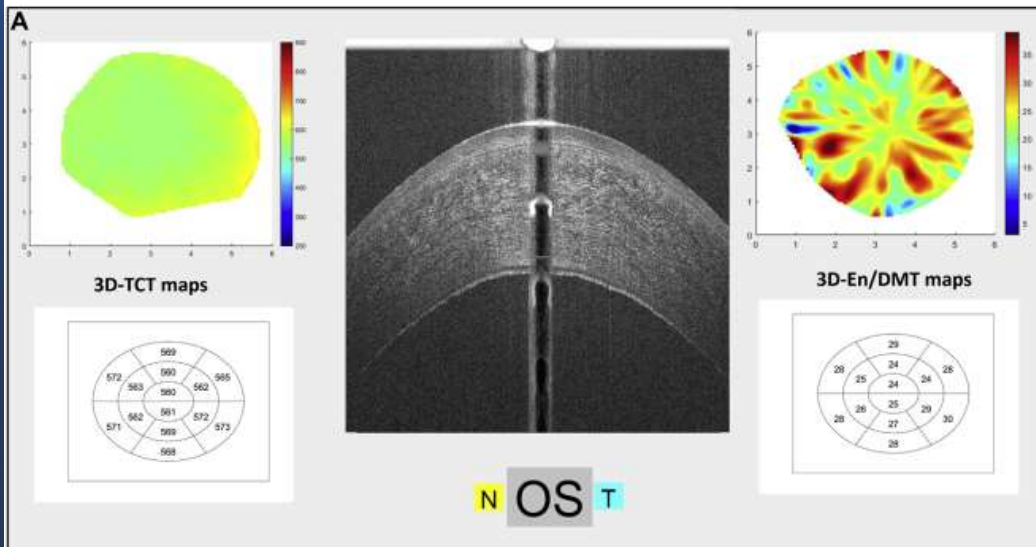
 Article Info

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Eleiwa *et al* • Endothelium-DM Thickness in Fuchs' Dystrophy



## Questions



1- Are there significant **regional** changes in En/DMT in graft rejection?

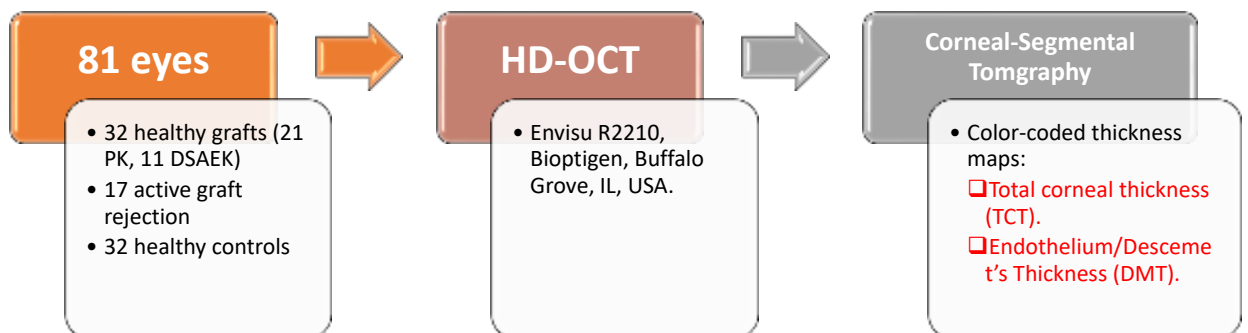
**If yes,**

2- Is it more reliable than Total corneal thickness?

3- PREDICTION?



## Cross-sectional study



## Results

- Q1:
  - Both regional TCT and En/DMT were significantly greater in actively rejecting grafts compared to both healthy corneas and clear grafts ( $P < 0.001$ ).



Q2: En/DMT Vs. TCT?

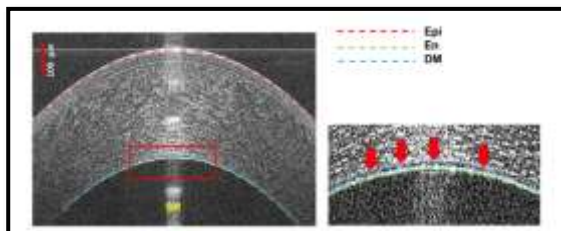
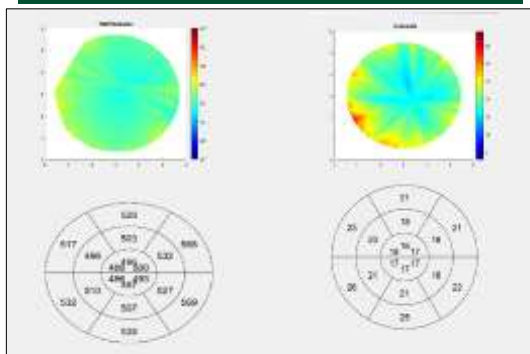


## 3D-Endothelium/Descemet's Thickness Maps

- Case 1: Healthy cornea

3D-TCT Map

3D-En/DM Map

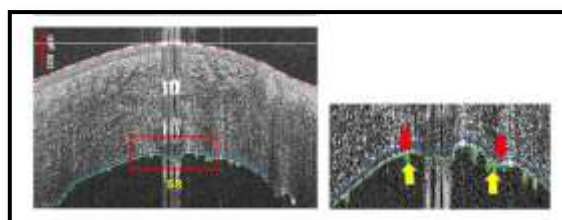
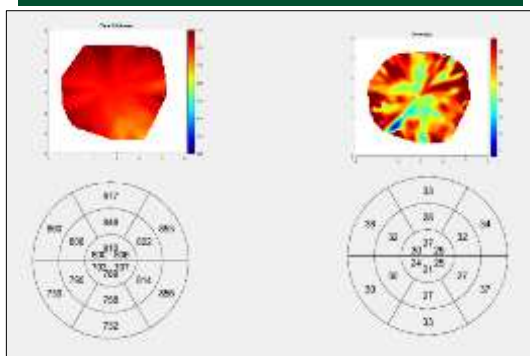


## 3D-Endothelium/Descemet's Thickness Maps

- Case 2: Active Graft Rejection

3D-TCT Map

3D-En/DM Map

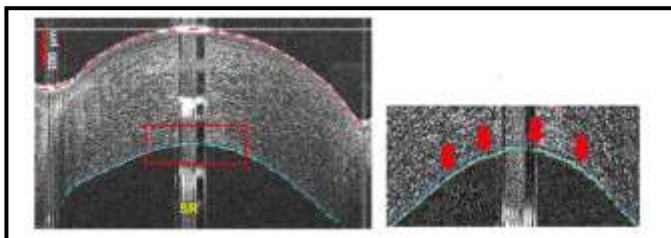
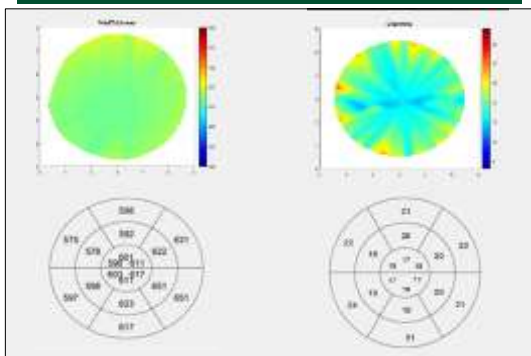


## 3D-Endothelium/Descemet's Thickness Maps

- Case 3: Healthy Corneal Graft (Thick graft)

3D-TCT Map

3D-En/DM Map

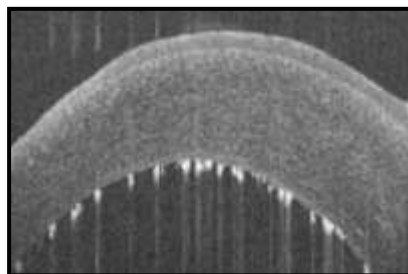
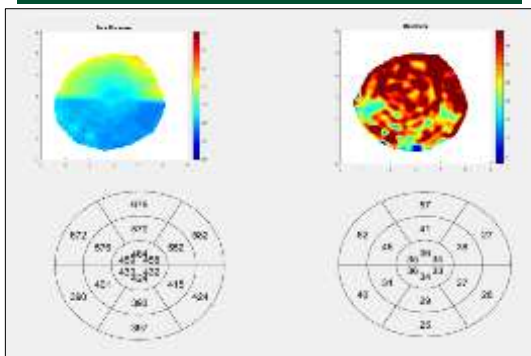


## 3D-Endothelium/Descemet's Thickness Maps

- Case 4: Active Graft Rejection (Thin graft)

3D-TCT Map

3D-En/DM Map



**C**  
**E**  
**F**



American Journal of Ophthalmology  
Volume 210, February 2020, Pages 48-58



Original Article

## Diagnostic Performance of Three-Dimensional Endothelium/Descemet Membrane Complex Thickness Maps in Active Corneal Graft Rejection

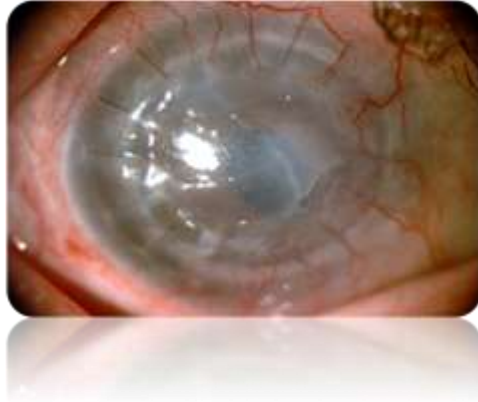
Taher K. Eleiwa<sup>a, b</sup>, Jane C. Cook<sup>a</sup>, Amr S. Elsayy<sup>a, c</sup>, Vatookarn Roongpoovapatr<sup>a</sup>, Vincent Volante<sup>a</sup>, Sonia Yoo<sup>a</sup>, Mohamed Abou Shousha<sup>a, c, d</sup>  

NEXT



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## Q3: Predictive role?



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## Prospective series of 31 patients

### 31 high-risk corneal transplants

- 14 repeat grafts
- 7 Therapeutic grafts
- 4 corneal scarring secondary to herpetic eye disease
- 4 Pseudophakic Bullous Keratopathy with vascularized bed
- 1 Stevens–Johnson syndrome
- 1 Congenital Hereditary Endothelial Dystrophy

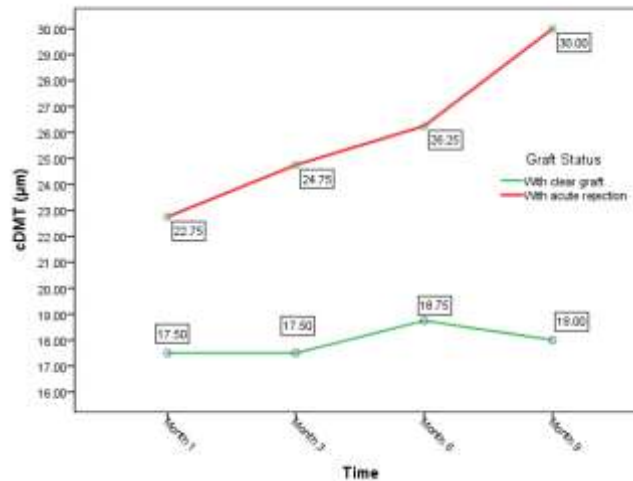
### Type of the transplant

- 23 PK
- 6 DSAEK
- 2 DSAEK under PK

### HD-OCT

- POM#1
- POM#3
- POM#6
- POM#9
- POM#12

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In patients with graft rejection (35.5%), the **cDMT** increased significantly **4.7 months (95%CI: 2.8-6.6)** prior to the clinical diagnosis of graft rejection, while it remained stable in patients without GR.

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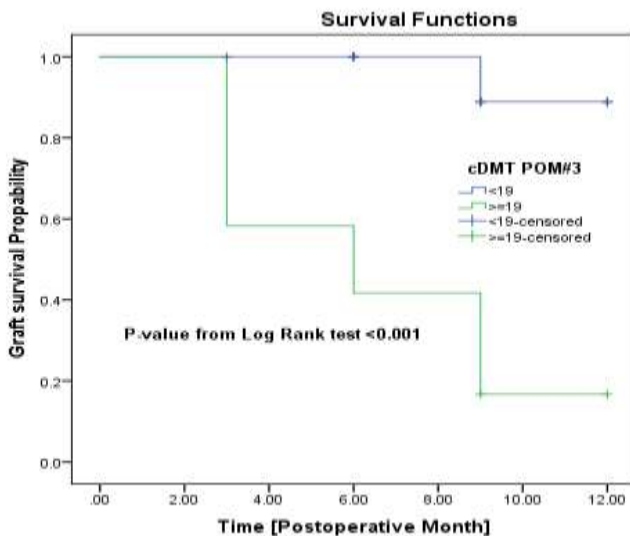


Fig. 2: 1-year cumulative incidence of GR

The 1-year cumulative incidence of graft rejection was:

- **83.3%** (hazard ratio = 18, 95% CI: 2-144) in patients with a **3-month cDMT  $\geq 19\mu\text{m}$ ,**
- **11.1%** for **cDMT  $< 19\mu\text{m}$**  (P < 0.001, fig. 2).

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### **Prediction of corneal graft rejection using central endothelium/Descemet's membrane complex thickness in high-risk corneal transplants**

[Taher Eleiwa](#), [Amr Elsayy](#), [Eyup Ozcan](#), [Collin Chase](#), [William Feuer](#), [Sonia H. Yoo](#), [Victor L. Perez](#) & [Mohamed F. Abou Shousha](#) 



## Take home message

Do AS-OCT for your high-risk corneal transplant patients



