# Nuovi scenari in Oftalmologia tra innovazione e sostenibilità
## Alghero 19-20 Maggio 2017

# *Il ruolo dell'epitelio nella diagnosi precoce delle ectasie corneali*

## Le distrofie e le degenerazioni corneali
## Moderatori: P. Pintore – F. Zanetti – M. Fossarello – F. Boscia – A. Pinna







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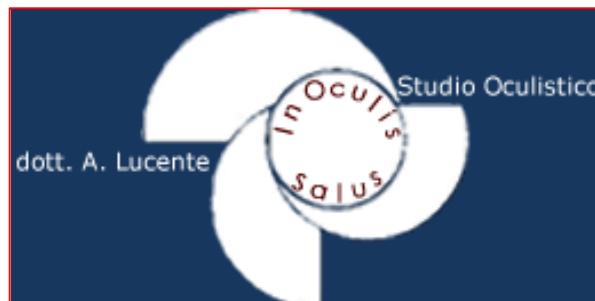
# Disclosure

*Consulting Free:*

*- Carl Zeiss Meditec*

*- Alfa Intes*

# Epithelial and stromal thickness maps
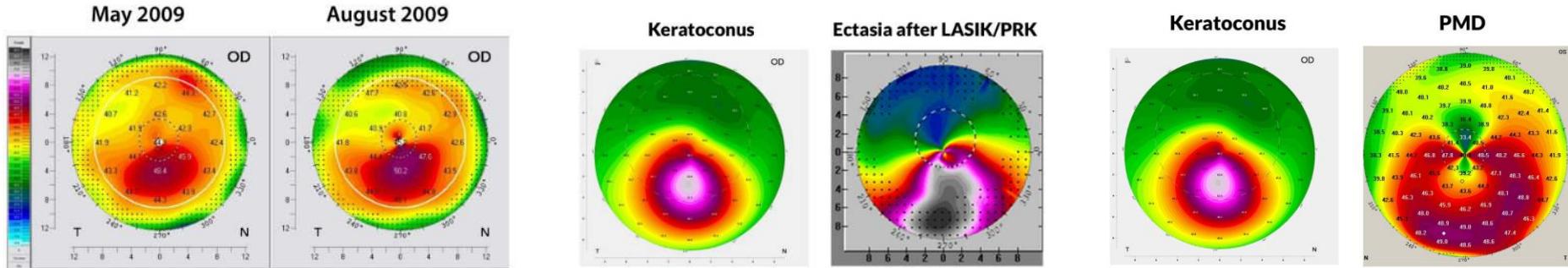


Reinstein DZ è stato il primo a pubblicare nel **1994** le mappe di spessore epiteliale oltre i 3 mm centrali di diametro utilizzando gli ultrasuoni ad alta frequenza con imaging tridimensionale.

*Reinstein DZ, Silverman RH, Trokel SL, Coleman DJ. Corneal pachymetric topography. **Ophthalmology. 1994;101:432-438***

- **Kanellopoulos AJ et al**. hanno studiato nel **2013** la distribuzione delle mappe di spessore dell'epitelio corneale in 373 soggetti normali (737 casi)

- **Spessore Medio: 53.28 ± 3.34 µm** (range 45-60 µm)

*Kanellopoulos AJ, Moustou V, Asimellis G. Evaluation of visual acuity, pachymetry and anterior-surface irregularity in keratoconus and crosslinking intervention follow-up in 737 cases. J Kerat Ect Cor Dis. **2013**;2(3):95–103.*

# Epithelial Remodelling

- Dan Z. Reinstein et al.:Diagnosing Keratoconus Using VHF Digital Ultrasound Epithelial Thickness Profiles, Essentials in Ophthalmology **29/12/16**

- Although these approaches have improved the effectiveness of keratoconus screening, there still remain equivocal cases where a confident diagnosis cannot be made and **undiagnosed keratoconus** remains probably the leading **cause** of corneal **ectasia after LASIK**

- The **corneal epithelium** has the ability to **alter its thickness profile** to reestablish a smooth, symmetrical optical outer corneal surface and either partially or totally **mask** the presence of an irregular stromal surface from front surface topography

**Epithelial Thickness Profile in Normal Eyes and Keratoconus**
5.7 μm thicker inferiorly than superiorly, and 1.2 μm thicker temporally than nasally
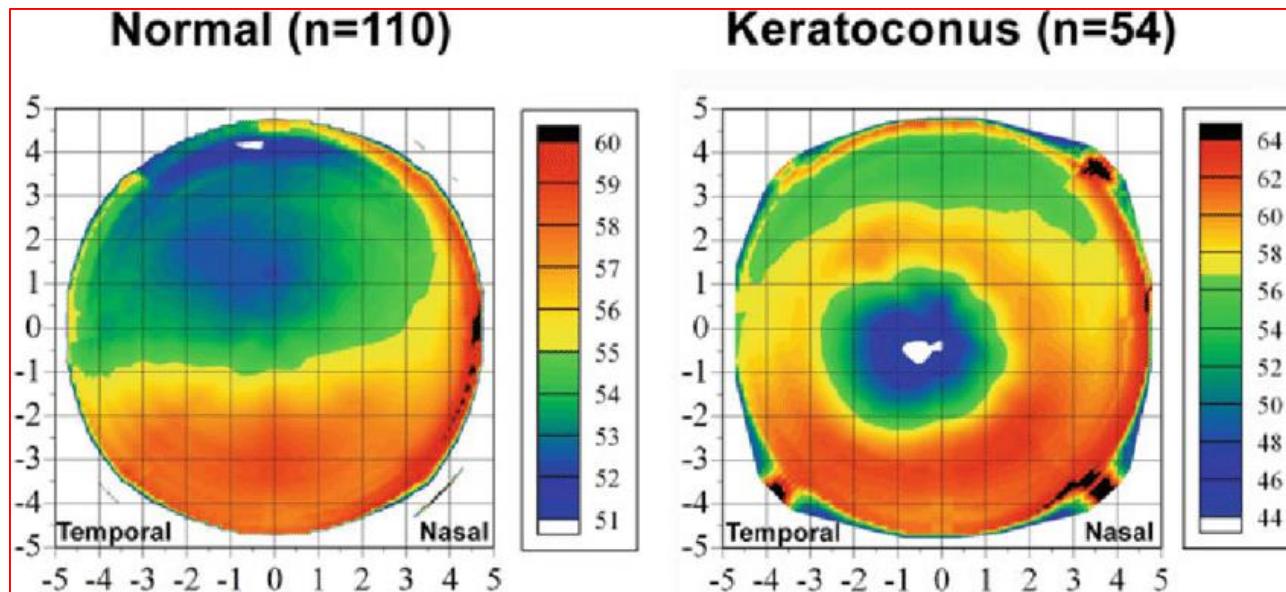
# Artemis-1 technology

Artemis very high-frequency digital ultrasound arc scanner;
(ArcScan Inc., Golden, CO) → **Broadband 50 MHz**
→ **10 mm diameter**
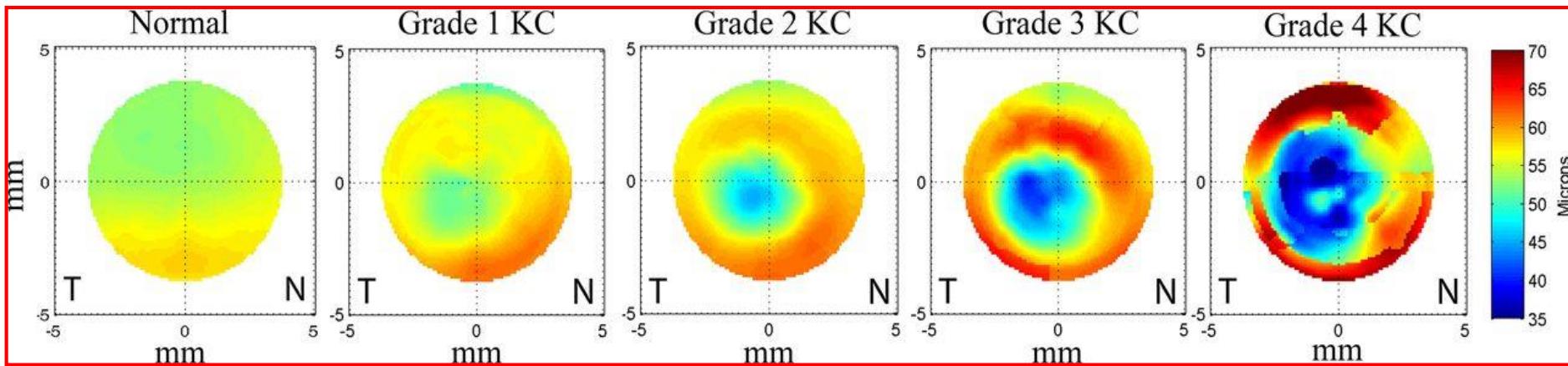


Epithelial thickness maps averaged over all normal corneas and each keratoconus (KC) grade. The departure from the normal epithelial distribution is evident even in grade 1 KC, but becomes more obvious with severity

# Epithelial Remodeling as Basis for Machine-Based Identification of Keratoconus

Ronald H. Silverman,[1,2] Raksha Urs,[1] Arindam RoyChoudhury,[3] Timothy J. Archer,[4] Marine Gobbe,[4] and Dan Z. Reinstein[1,4,5]

[1]Department of Ophthalmology, Columbia University Medical Center, New York, New York
[2]F. L. Lizzi Center for Biomedical Engineering, Riverside Research, New York, New York
[3]Department of Biostatistics, Columbia University Medical Center, New York, New York
[4]London Vision Clinic, London, United Kingdom
[5]Centre Hospitalier National d'Ophtalmologie des Quinze-Vingts, Paris, France

Normal

Epithelial Thickness — Stromal Thickness

Keratoconus

Epithelial Thickness — Stromal Thickness

Examples of epithelial and stromal thickness maps for a representative normal and a keratoconus cornea. The horizontal (x) scale is plotted from temporal (T) to nasal (N).
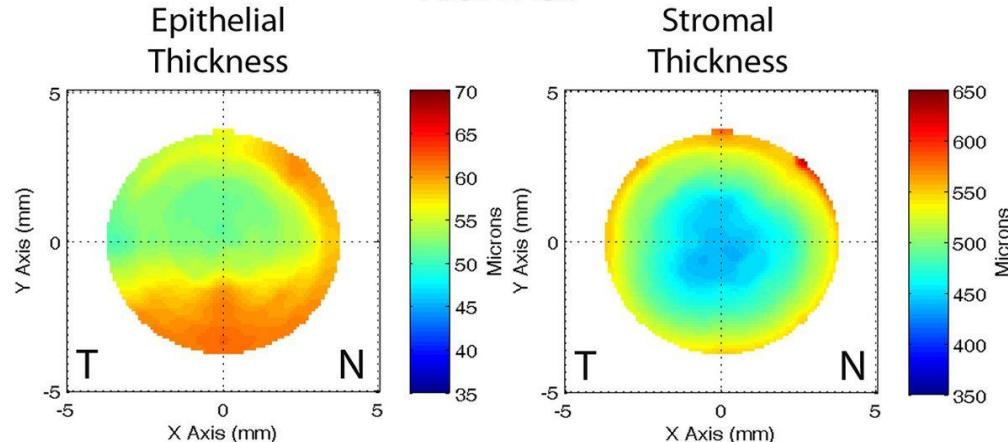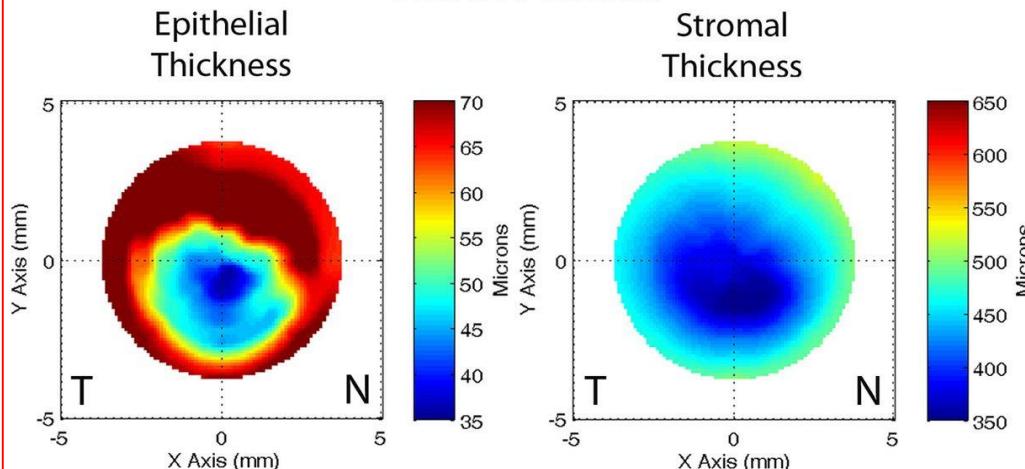
In the **normal eye, the epithelium** is somewhat **thickened inferiorly** to a **maximum** of approximately **60 µm**, with **central thickness** of approximately **52 µm.** The **stroma is thinnest centrally.**

In the **keratoconus eye**, a prominent epithelial defect is located **1 mm inferior to center,** with the epithelium measuring only **35 µm.**

**The epithelium** thickens **concentrically** about the defect, reaching a maximum of **70 µm** superiorly. **The stroma** shows a defect coincident with the position of the epithelial defect, where it is approximately **350 µm** in thickness.

- *Central keratometry*

*- Atlas corneal topography and PathFinder™ corneal analysis*

- *Orbscan anterior and posterior elevation BFS*

- *Artemis epithelial thickness profile*

for one normal eye, one keratoconic eye, and three example eyes where the diagnosis of keratoconus might be misleading from topography.
The final diagnosis based on the epithelial thickness profile is shown at the bottom of each example
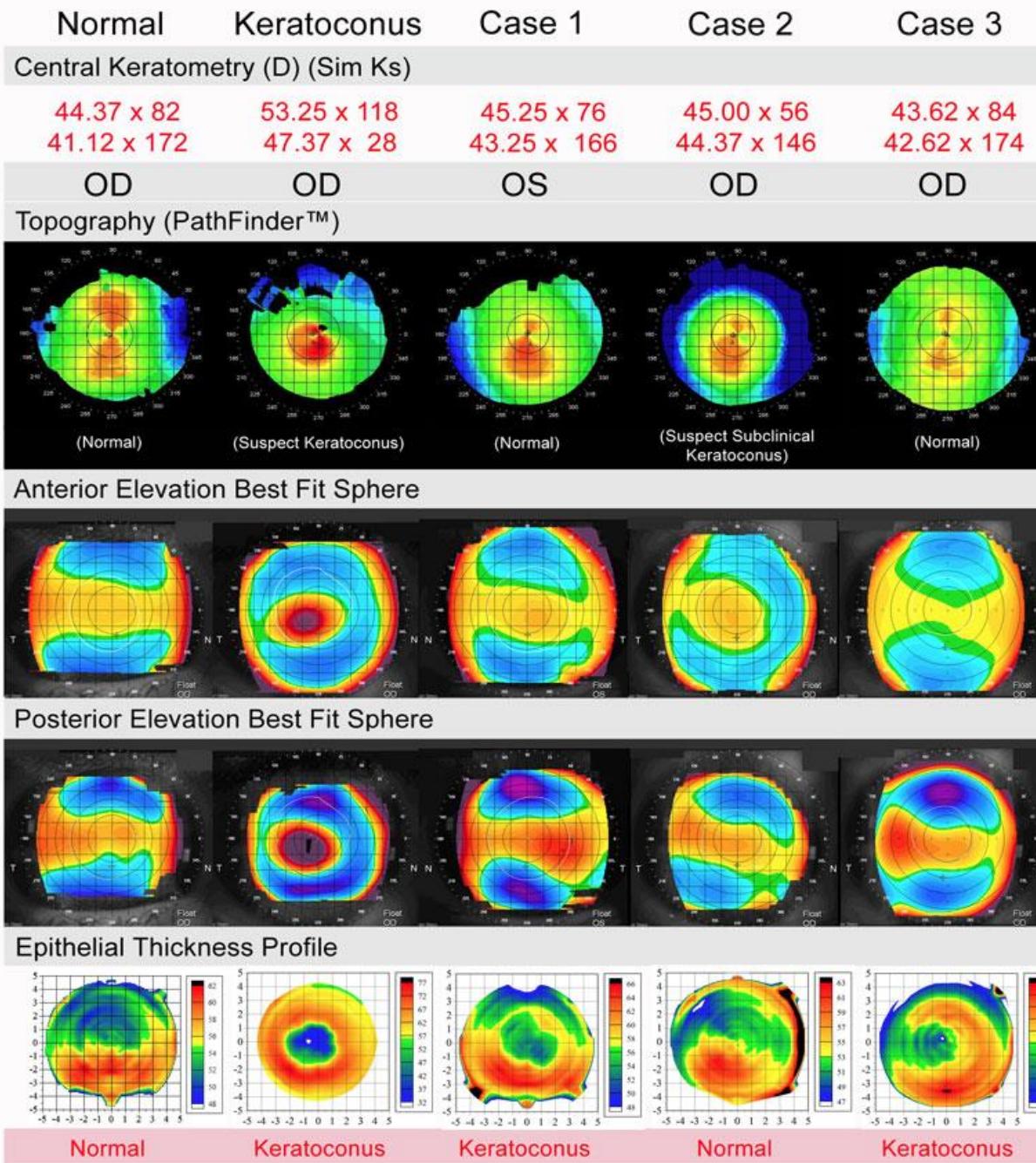
| | Normal | Keratoconus | Case 1 | Case 2 | Case 3 |
|---|---|---|---|---|---|
| Central Keratometry (D) (Sim Ks) | | | | | |
| | 44.37 x 82 | 53.25 x 118 | 45.25 x 76 | 45.00 x 56 | 43.62 x 84 |
| | 41.12 x 172 | 47.37 x 28 | 43.25 x 166 | 44.37 x 146 | 42.62 x 174 |
| | OD | OD | OS | OD | OD |
| Topography (PathFinder™) | (Normal) | (Suspect Keratoconus) | (Normal) | (Suspect Subclinical Keratoconus) | (Normal) |
| Anterior Elevation Best Fit Sphere | | | | | |
| Posterior Elevation Best Fit Sphere | | | | | |
| Epithelial Thickness Profile | Normal | Keratoconus | Keratoconus | Normal | Keratoconus |

**ZEISS**

## Analisi di Pachimetria : Pachimetria

OD ● | ● OS

### Pachimetria



### Spessore dell'epitelio



Passaggio 20 µm

### Pachimetria OD
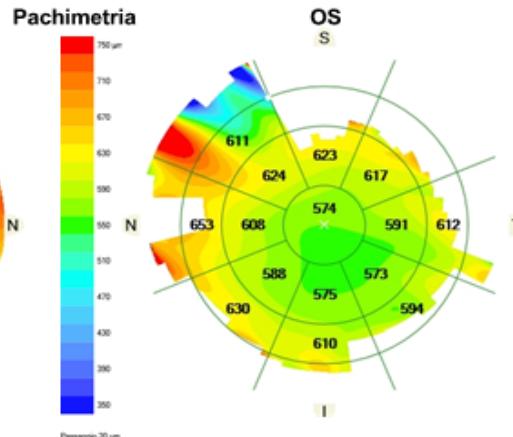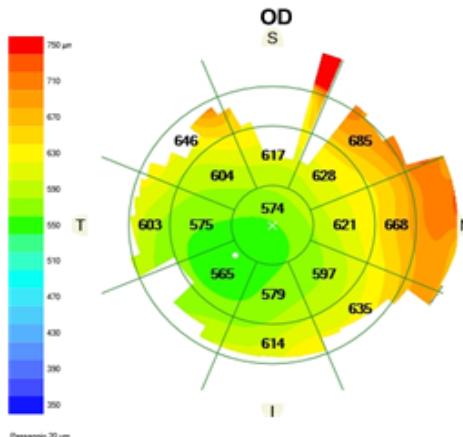
| Intervallo (mm) | Min. (µm) | Media (µm) | Max. (µm) | S-I (µm) | SN-IT (µm) |
|---|---|---|---|---|---|
| 0,0-2,0 | 558 | 574 | 600 | - | - |
| 2,0-5,0 | 558 | 598 | 662 | 38 | 63 |
| 5,0-7,0 | 576 | 642 | 726 | - | - |

| Minimo Spessore (µm) | 558 | Y Min (µm) | -773 |
|---|---|---|---|
| Pachy Min-Medio (µm) | -38 | Vertice Spessore (µm) | 568 |

### Pachimetria OS

| Intervallo (mm) | Min. (µm) | Media (µm) | Max. (µm) | S-I (µm) | SN-IT (µm) |
|---|---|---|---|---|---|
| 0,0-2,0 | 558 | 574 | 599 | - | - |
| 2,0-5,0 | 558 | 600 | 665 | 48 | 51 |
| 5,0-7,0 | 467 | 618 | 735 | - | 17 |

| Minimo Spessore (µm) | 467 | Y Min (µm) | 3219 |
|---|---|---|---|
| Pachy Min-Medio (µm) | -39 | Vertice Spessore (µm) | 570 |

### Spessore dell'epitelio OD
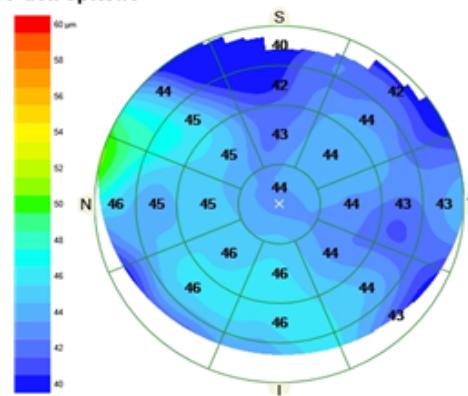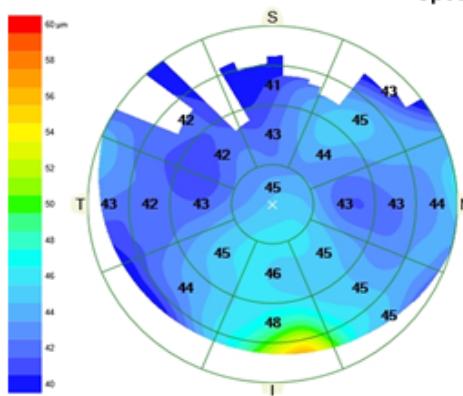
| Intervallo (mm) | Min. (µm) | Media (µm) | Max. (µm) | S-I (µm) | SN-IT (µm) |
|---|---|---|---|---|---|
| 0,0-2,0 | 43 | 45 | 46 | - | - |
| 2,0-5,0 | 41 | 44 | 47 | -3 | -1 |
| 5,0-7,0 | 38 | 44 | 53 | -7 | 1 |
| 7,0-9,0 | 39 | 44 | 51 | - | - |

| Minimo Spessore (µm) | 33 | Y min (mm) | 3,8 |
|---|---|---|---|
| Min-Medio (µm) | -3 | Spessore centrale (µm) | 45 |

### Spessore dell'epitelio OS

| Intervallo (mm) | Min. (µm) | Media (µm) | Max. (µm) | S-I (µm) | SN-IT (µm) |
|---|---|---|---|---|---|
| 0,0-2,0 | 44 | 44 | 46 | - | - |
| 2,0-5,0 | 42 | 45 | 47 | -3 | 1 |
| 5,0-7,0 | 39 | 44 | 48 | -4 | 1 |
| 7,0-9,0 | 36 | 43 | 51 | - | 1 |

| Minimo Spessore (µm) | 35 | Y min (mm) | 4,3 |
|---|---|---|---|
| Min-Medio (µm) | -3 | Spessore centrale (µm) | 44 |

Commenti

Firma del medico

## Analisi di Pachimetria : Pachimetria

OD ●   ● OS

### OD   Pachimetria   OS



Passaggio 20 µm   Passaggio 20 µm

### Spessore dell'epitelio



### Pachimetria OD

| Intervallo (mm) | Min. (µm) | Media (µm) | Max. (µm) | S-I (µm) | SN-IT (µm) |
|---|---|---|---|---|---|
| 0,0-2,0 | 546 | 555 | 571 | - | - |
| 2,0-5,0 | 546 | 563 | 609 | - | 25 |
| 5,0-7,0 | 543 | 581 | 649 | - | - |

| Minimo Spessore (µm) | 543 | Y Min (µm) | -3194 |
|---|---|---|---|
| Pachy Min-Medio (µm) | -500 | Vertice Spessore (µm) | 551 |

### Pachimetria OS

| Intervallo (mm) | Min. (µm) | Media (µm) | Max. (µm) | S-I (µm) | SN-IT (µm) |
|---|---|---|---|---|---|
| 0,0-2,0 | 487 | 516 | 549 | - | - |
| 2,0-5,0 | 485 | 549 | 620 | 64 | 73 |
| 5,0-7,0 | 581 | 618 | 675 | - | - |

| Minimo Spessore (µm) | 485 | Y Min (µm) | -869 |
|---|---|---|---|
| Pachy Min-Medio (µm) | -61 | Vertice Spessore (µm) | 513 |

### Spessore dell'epitelio OD
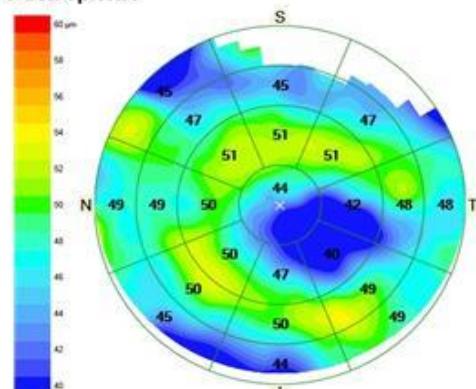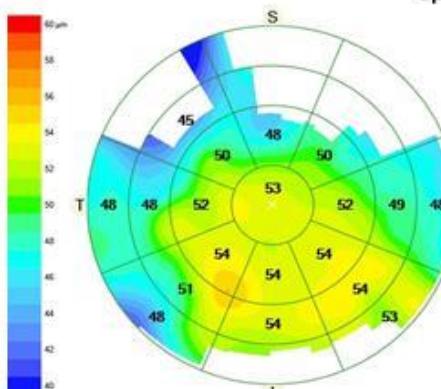
| Intervallo (mm) | Min. (µm) | Media (µm) | Max. (µm) | S-I (µm) | SN-IT (µm) |
|---|---|---|---|---|---|
| 0,0-2,0 | 51 | 53 | 54 | - | - |
| 2,0-5,0 | 45 | 52 | 56 | -6 | -4 |
| 5,0-7,0 | 42 | 50 | 56 | - | - |
| 7,0-9,0 | 42 | 49 | 54 | - | - |

| Minimo Spessore (µm) | 35 | Y min (mm) | 4,0 |
|---|---|---|---|
| Min-Medio (µm) | -7 | Spessore centrale (µm) | 53 |

### Spessore dell'epitelio OS

| Intervallo (mm) | Min. (µm) | Media (µm) | Max. (µm) | S-I (µm) | SN-IT (µm) |
|---|---|---|---|---|---|
| 0,0-2,0 | 37 | 44 | 52 | - | - |
| 2,0-5,0 | 36 | 48 | 54 | 4 | 11 |
| 5,0-7,0 | 40 | 48 | 55 | -5 | -2 |
| 7,0-9,0 | 35 | 47 | 54 | - | -4 |

| Minimo Spessore (µm) | 32 | Y min (mm) | 3,4 |
|---|---|---|---|
| Min-Medio (µm) | -11 | Spessore centrale (µm) | 43 |

Commenti

Firma del medico

| Nome: | **CL** | | OD | OS | Studio Oculistico A. Lucente |
|---|---|---|---|---|---|
| ID: | CZMI407946366 | Data esame: | 19/05/2016 | 19/05/2016 | |
| Data di nascita: | | Ora dell'esame: | 17:03 | 17:04 | |
| Sesso: | Unknown | Numero di serie: | 5000-6254 | 5000-6254 | |
| Tecnico: | Angio, Cirrus | Intensità segnale: | N/D | N/D | |

## Analisi di Pachimetria : Pachimetria

OD ● | ● OS

### Pachimetria OD
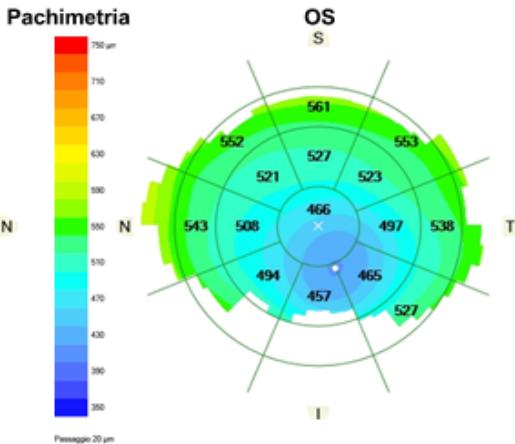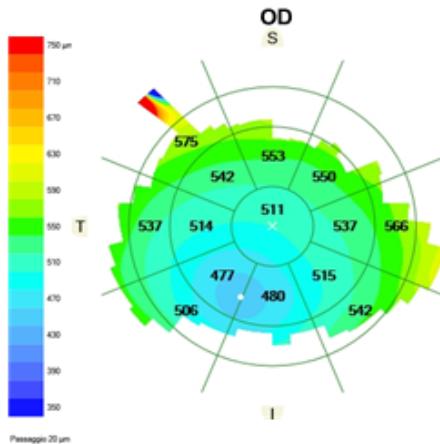
| Intervallo (mm) | Min. (µm) | Media (µm) | Max. (µm) | S-I (µm) | SN-IT (µm) |
|---|---|---|---|---|---|
| 0,0-2,0 | 481 | 511 | 529 | - | - |
| 2,0-5,0 | 461 | 521 | 586 | 73 | 73 |
| 5,0-7,0 | 471 | 545 | 624 | - | - |

| | | | |
|---|---|---|---|
| Minimo Spessore (µm) | 461 | Y Min (µm) | -1767 |
| Pachy Min-Medio (µm) | -59 | Vertice Spessore (µm) | 511 |

### Pachimetria OS

| Intervallo (mm) | Min. (µm) | Media (µm) | Max. (µm) | S-I (µm) | SN-IT (µm) |
|---|---|---|---|---|---|
| 0,0-2,0 | 429 | 466 | 505 | - | - |
| 2,0-5,0 | 429 | 499 | 545 | 70 | 56 |
| 5,0-7,0 | 499 | 546 | 581 | - | 25 |

| | | | |
|---|---|---|---|
| Minimo Spessore (µm) | 429 | Y Min (µm) | -1050 |
| Pachy Min-Medio (µm) | -66 | Vertice Spessore (µm) | 460 |

### Spessore dell'epitelio OD
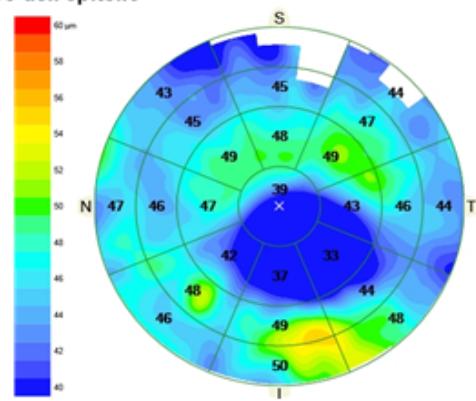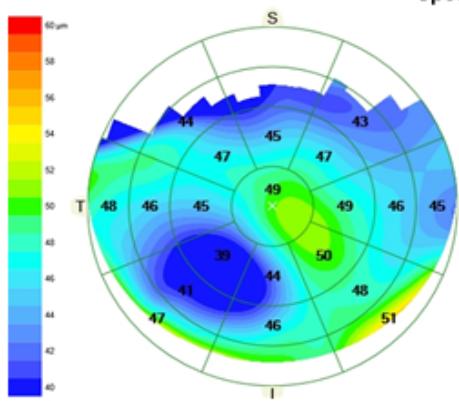
| Intervallo (mm) | Min. (µm) | Media (µm) | Max. (µm) | S-I (µm) | SN-IT (µm) |
|---|---|---|---|---|---|
| 0,0-2,0 | 44 | 49 | 52 | - | - |
| 2,0-5,0 | 36 | 46 | 52 | 1 | 8 |
| 5,0-7,0 | 32 | 45 | 50 | - | 2 |
| 7,0-9,0 | 37 | 48 | 56 | - | - |

| | | | |
|---|---|---|---|
| Minimo Spessore (µm) | 16 | Y min (mm) | 2,2 |
| Min-Medio (µm) | -10 | Spessore centrale (µm) | 51 |

### Spessore dell'epitelio OS

| Intervallo (mm) | Min. (µm) | Media (µm) | Max. (µm) | S-I (µm) | SN-IT (µm) |
|---|---|---|---|---|---|
| 0,0-2,0 | 30 | 39 | 49 | - | - |
| 2,0-5,0 | 30 | 44 | 51 | 11 | 16 |
| 5,0-7,0 | 37 | 46 | 56 | -4 | 1 |
| 7,0-9,0 | 38 | 46 | 56 | - | -5 |

| | | | |
|---|---|---|---|
| Minimo Spessore (µm) | 30 | Y min (mm) | -0,9 |
| Min-Medio (µm) | -13 | Spessore centrale (µm) | 37 |

**Pachimetria**

OD — Passaggio 20 µm
OS — Passaggio 20 µm

**Spessore dell'epitelio**

| Commenti | Firma del medico | CIRRUS ANGIO |
|---|---|---|

CIRRUS ANGIO
SW Ver: 10.0.0.14618
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# Best parameter for documenting disease progression

- **Parameter 1: Anterior Corneal Surface**
"Will not show changes on the anterior surface until later the disease process"

- **Parameter 2: Epithelial Thickness**
" Is no published literature exploring the progression of disease with relation to epithelial thickness"

- **Parameter 3: BCVA**
"Due to this variability, BCVA is not a reliable measure of keratoconus progression"

- **Parameter 4: Corneal Thickness**
"A full corneal thickness map does have good potential to document progression"

- **Parameter 5: Posterior Corneal Surface**
"Has strong potential for measuring disease progression"

R Ambrosio    M Berlin
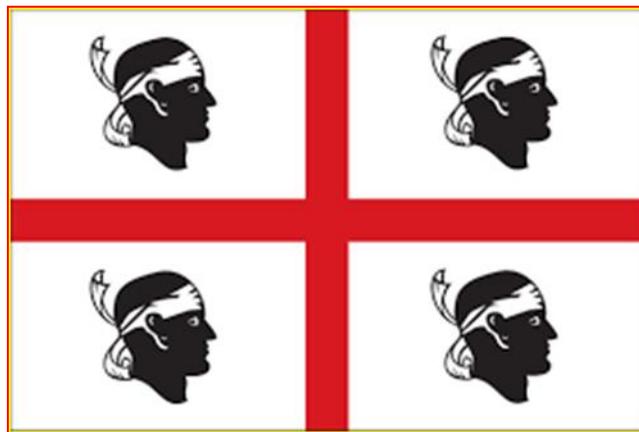
# Thank you for your kind attention



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