



Assistance Publique
Hôpitaux de Marseille




Quantification of human corneal graft transparency

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- **Context and problematic**
 - Tools for corneal transparency quantification
 - Performance of the proposed method and comparison
 - Application to corneal grafts
 - Conclusions and perspectives

Context and problematic

- The human cornea and its multiscale structure

Macrometric structure:

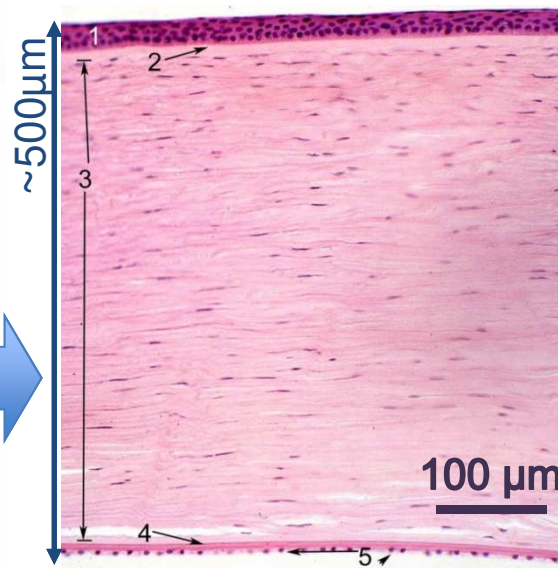
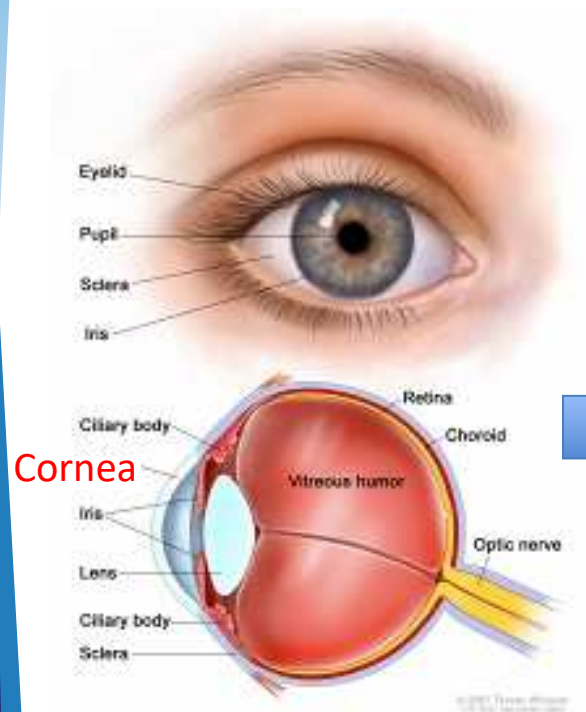
- Transmission

Micrometric structure:

- 5 layers

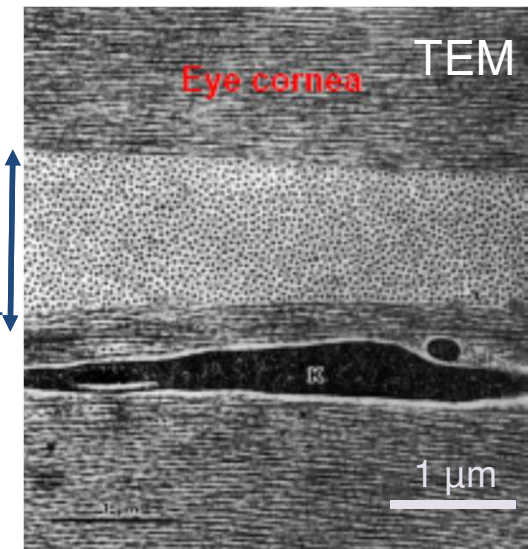
Nanometric structure:

- Organized fibrillar lamellas



Histological section of a cornea

- 1) Epithelium $\approx 50\mu\text{m}$
- 2) Bowman membrane $\approx 12\mu\text{m}$
- 3) **Stroma $\approx 450\mu\text{m}$**
- 4) Descemet membrane $\approx 5\mu\text{m}$
- 5) Endothelium $\approx 5\mu\text{m}$

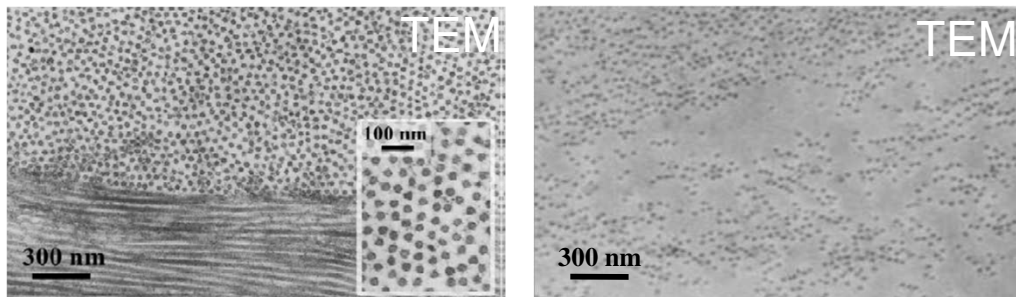


V. Tuchin. Tissue Optics

Context and problematic

Loss of transparency: Case of an edema

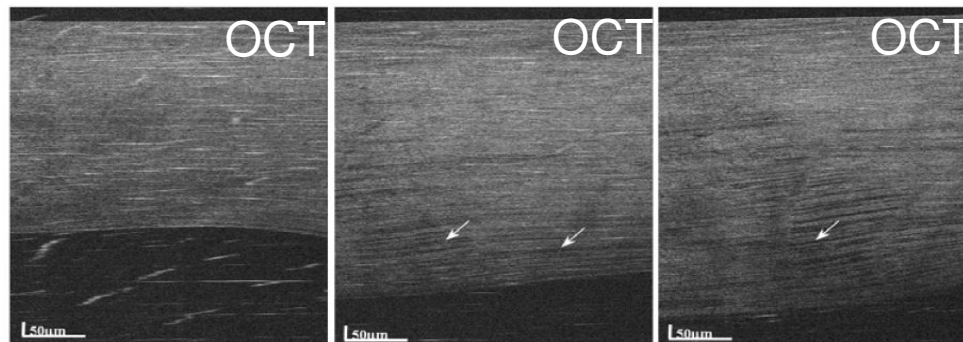
Nanometric scale



Disorganisation of the fibrillar lattice
▶ increase of the scattering

C. Crotti. thèse de doctorat, 2011
JL. Cox et al. J.Physiol. 210 (1970)

Micrometric scale



Detachment of the lamellas
▶ apparition of water lakes
▶ increase of the thickness and of the scattering

O. Casadessus et al. Biomedical Optic Express. (2012) Vol 3, No. 8

Macroscopic scale



Opacification of the cornea
Increase of the scattering


Context and problematic

Objectives

- Quantification of corneal transparency
- Access to smaller scale structure than the existing tools
- Precocious diagnosis of a variation of transparency



Proposed method: **Angular-Resolved Scattered Light Intensity** measurement in the reflected space

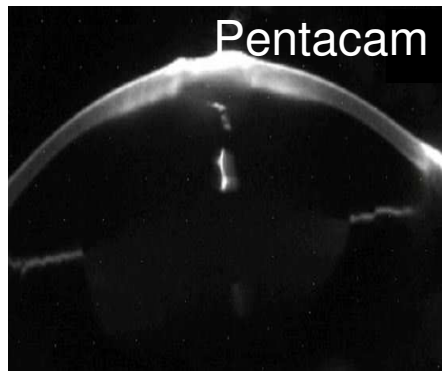
- 
- Context and problematic
 - **Tools for corneal transparency quantification**
 - Performance of the proposed method and comparison
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 - Conclusions and perspectives

Tools for corneal transparency quantification

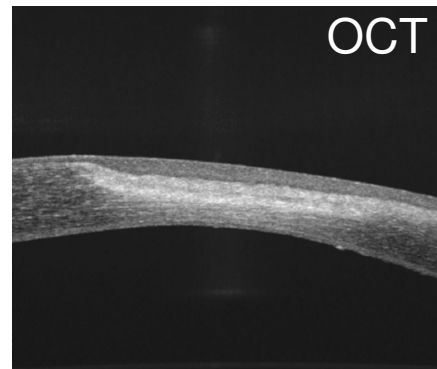
IN-VIVO

Quantification of transparency

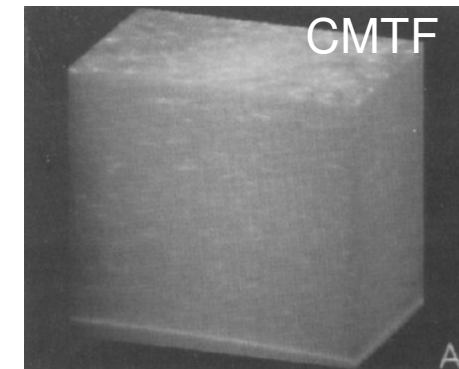
- Pentacam®
- Optical Coherence Tomography (OCT)
- Confocal Microscopy Through Focusing (CMTF)



Ahmad Muneer Otri et al.
Ophthalmology (2012) 119:501–508



J.S. Rose et al. *Journal of Current Ophthalmology* (2017) 1-4



T. Moller-Pedersen et al.
Ophthalmology (1997) 104:360-368

Used in hospitals

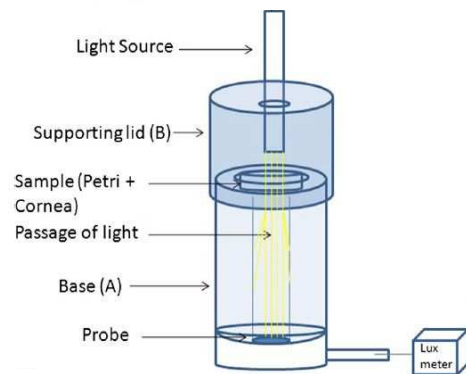
Used in research

Tools for corneal transparency quantification

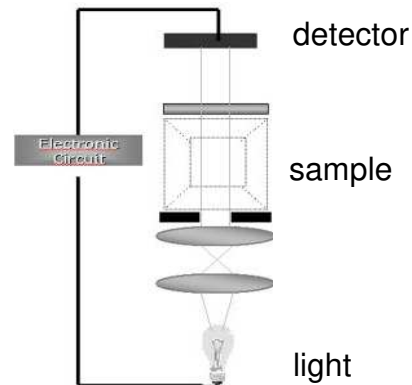
EX-VIVO

Quantification of transparency

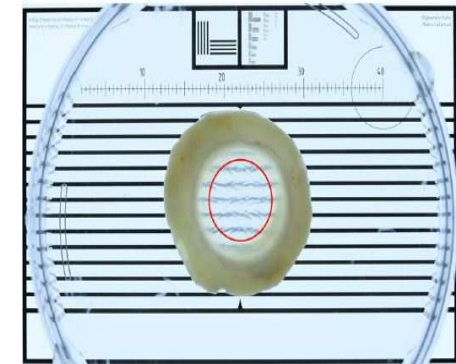
- Direct measurement of the transmitted light
- Modulation Transfer Function principle (MTF)



Mohit Parekhet et al. Cell Tissue Bank (2014) 15:7–13



L. Ventura et al. BioMedical Engineering OnLine (2005) 4:70



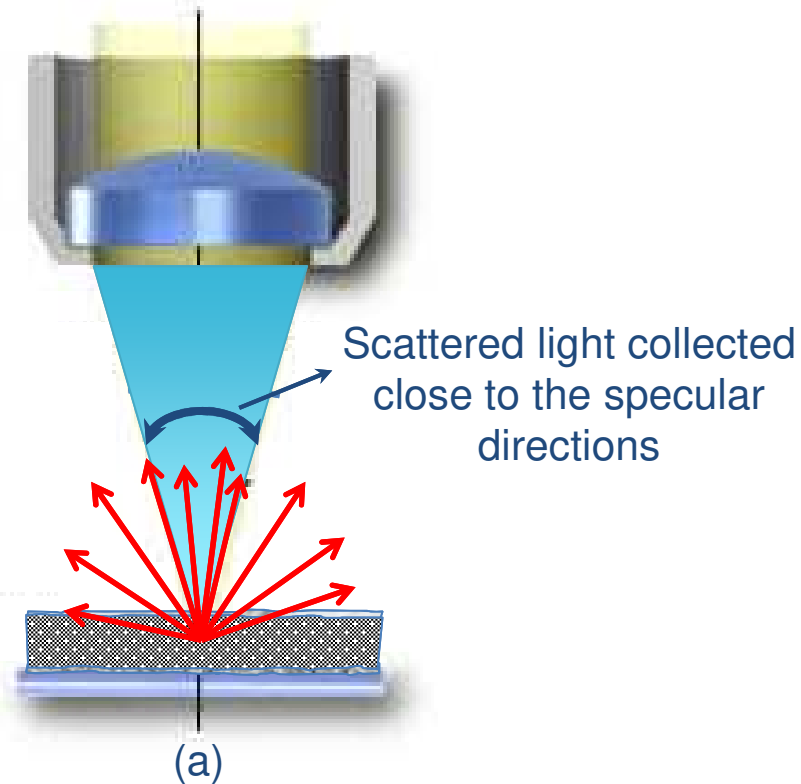
S. Acquart et al. Cell Tissue Bank (2014) 15:471–482

Used in Eye Bank tissue and in research

Tools for corneal transparency quantification

Limit of quantification tools

Accessible scale depends on the range $[\theta_{\min}; \theta_{\max}]$ measured



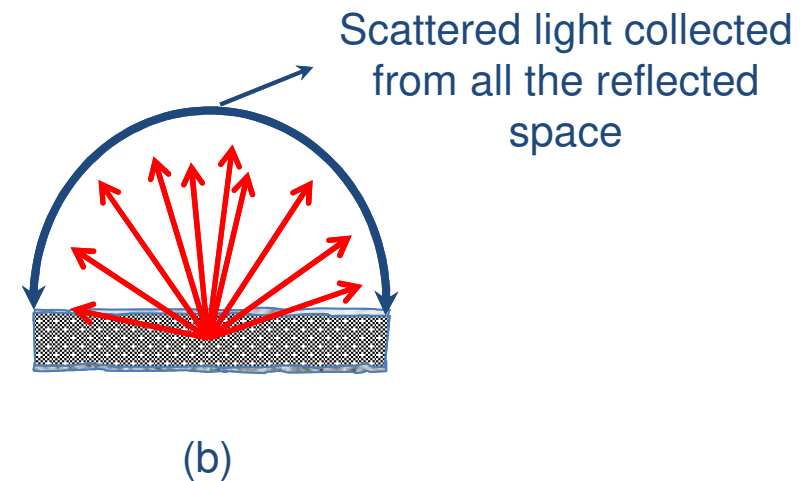
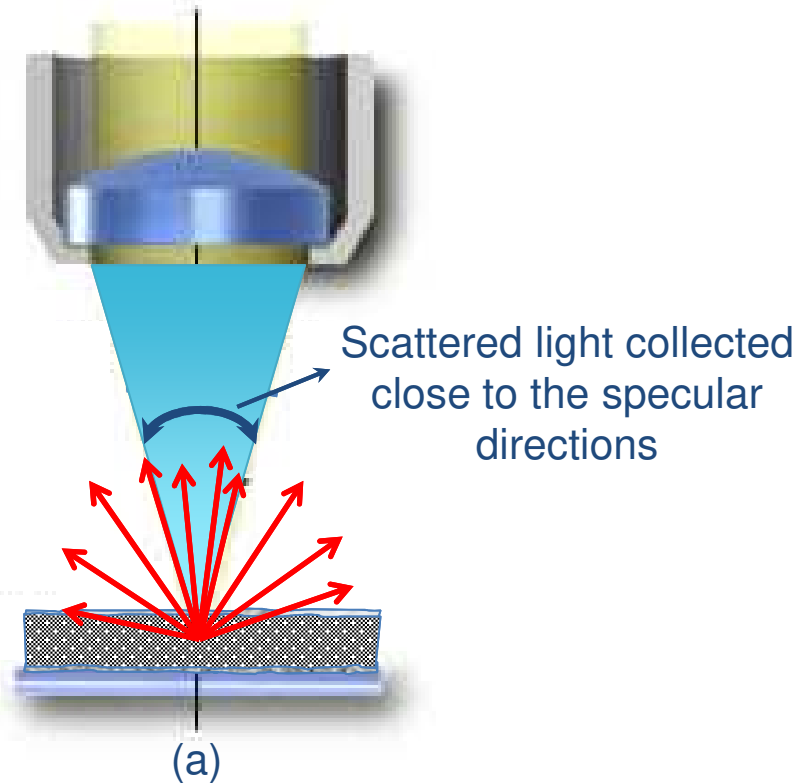
Actual quantification tools:

- Limit in the range of accessible angles
- Limit the resolution

Tools for corneal transparency quantification

Limit of quantification tools

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Actual quantification tools:

- Limit in the range of accessible angles
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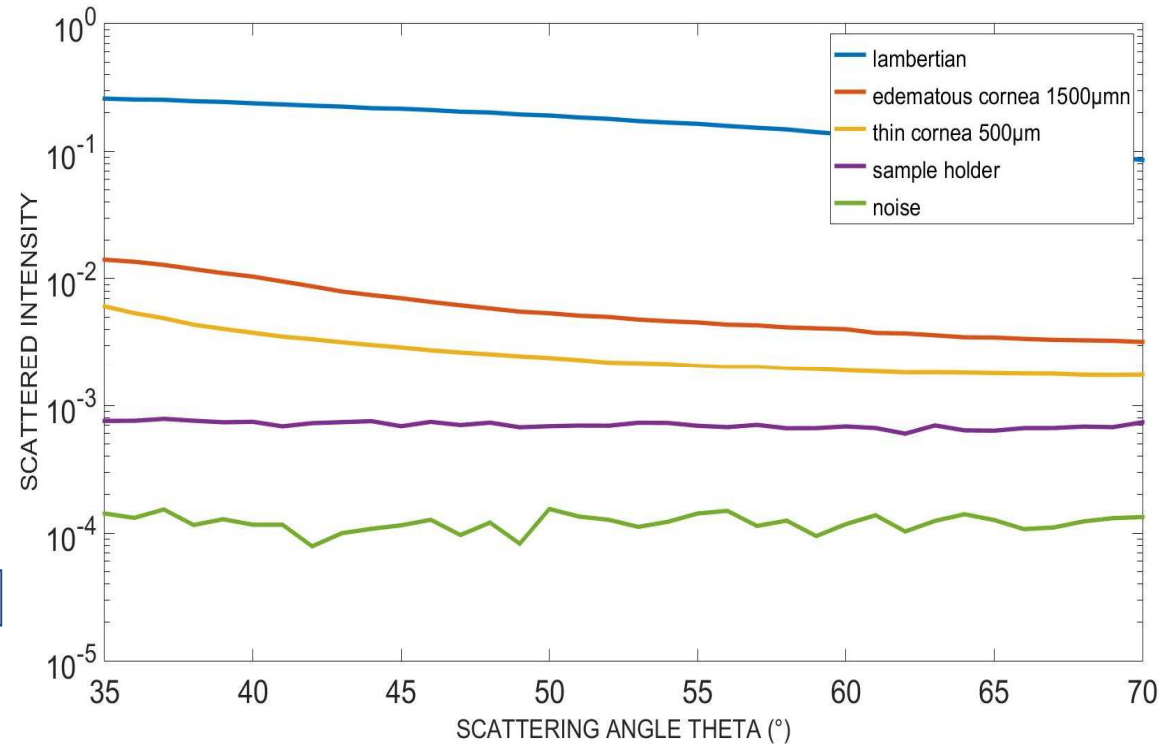
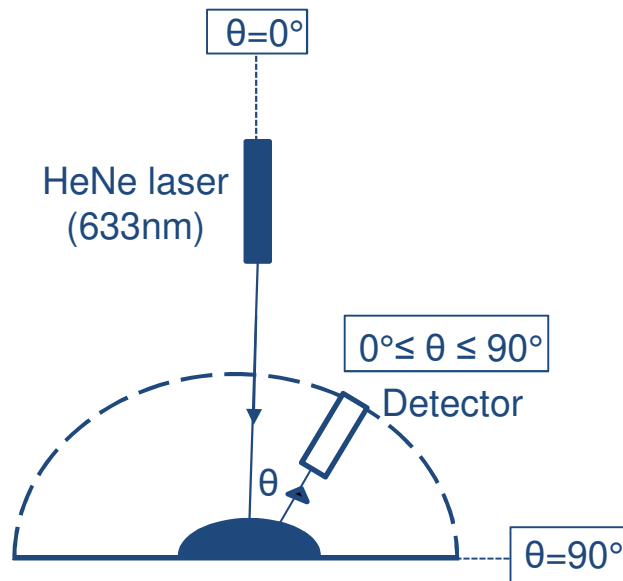
Proposed system:

- Access to a larger range of angles
- Access to a smaller scale structure

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Performance of the method and comparison

Experimental tools: Angular-resolved scattered measurement



Advantages:

- Access to more information coming from the bulk
- Better dynamic

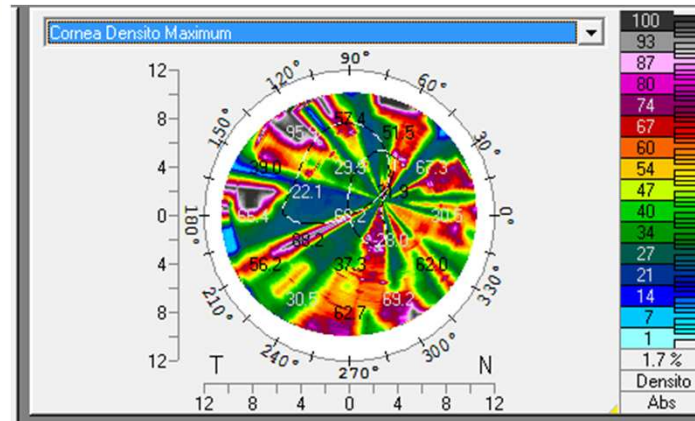
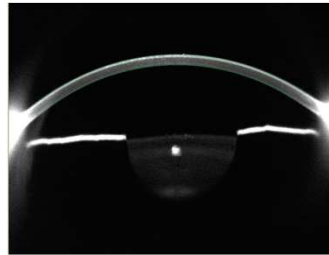
Total Integrated Scattering

$$\text{TIS} = \iint_{\theta, \varphi} I(\theta, \varphi) \sin \theta d\theta d\varphi$$

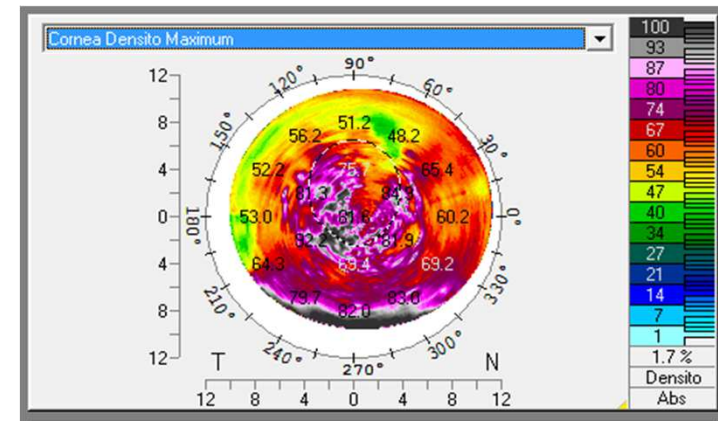
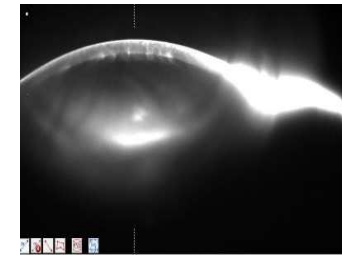
Performance of the method and comparison

Experimental tools: Pentacam

- Corneal topographer
- Resolution $\approx 10\mu\text{m}$
- Gives access to: thickness, topography, densitometry
- Densitometry: mean image brightness expressed as a percent (0–100)



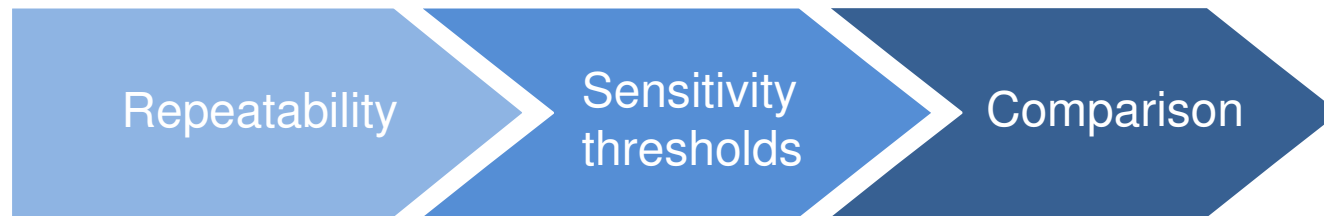
Healthy cornea



Edematous cornea

Performance of the method and comparison

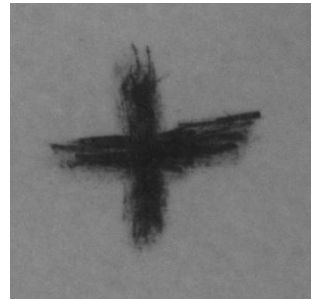
Protocol and method



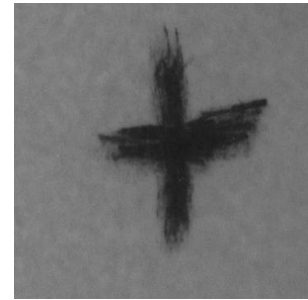
Calibrated samples: Agar - Agar phantoms
Fabricated with concentration from 1% to 3.5% with a step 0.1%



Agar-Agar
Concentration: 1%



Agar-Agar
Concentration: 2%



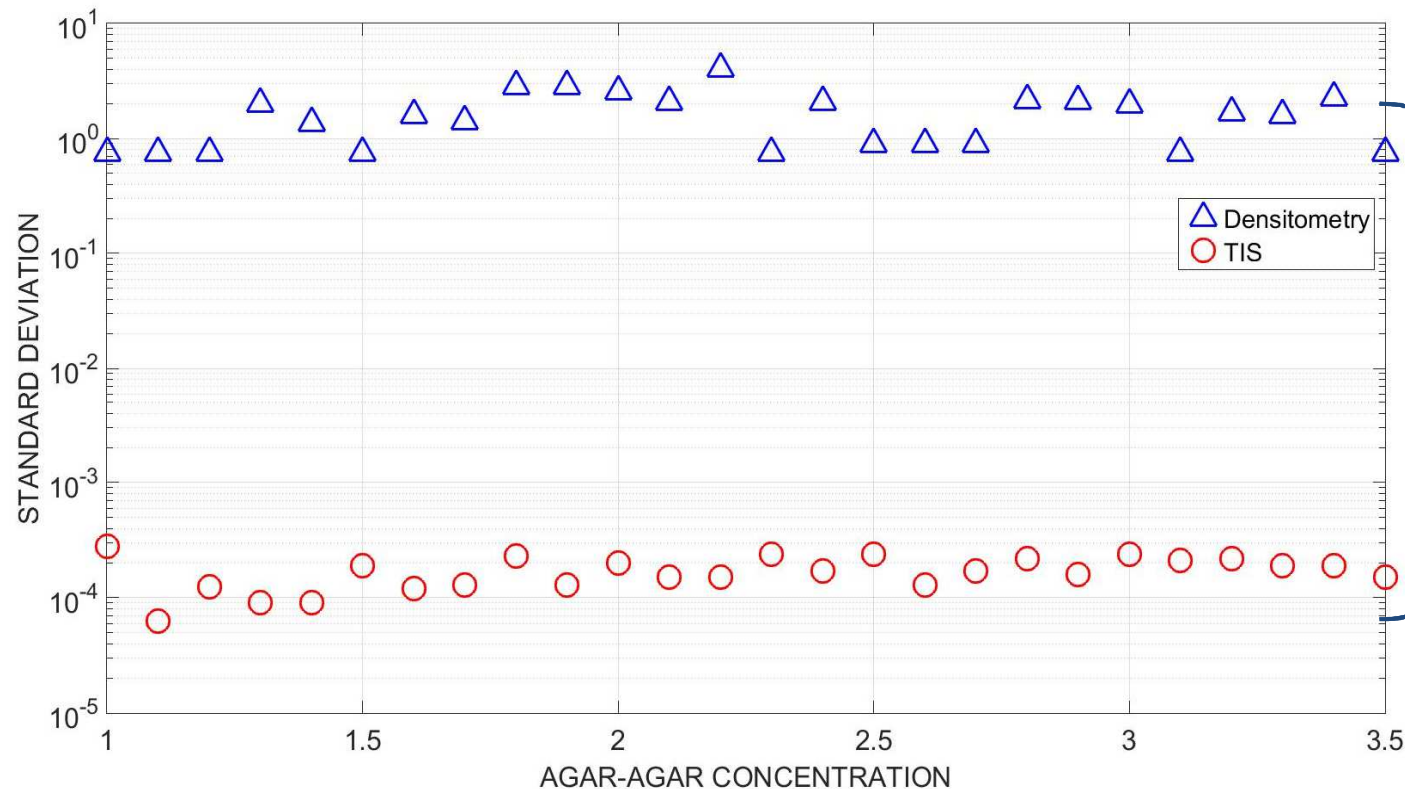
Agar-Agar
Concentration: 3.5%

Performance of the method and comparison

Repeatability

Repeatability

- Each Agar-Agar sample is measured five times in a row with both methods
- Calculation of the standard deviation of the TIS and of the densitometry



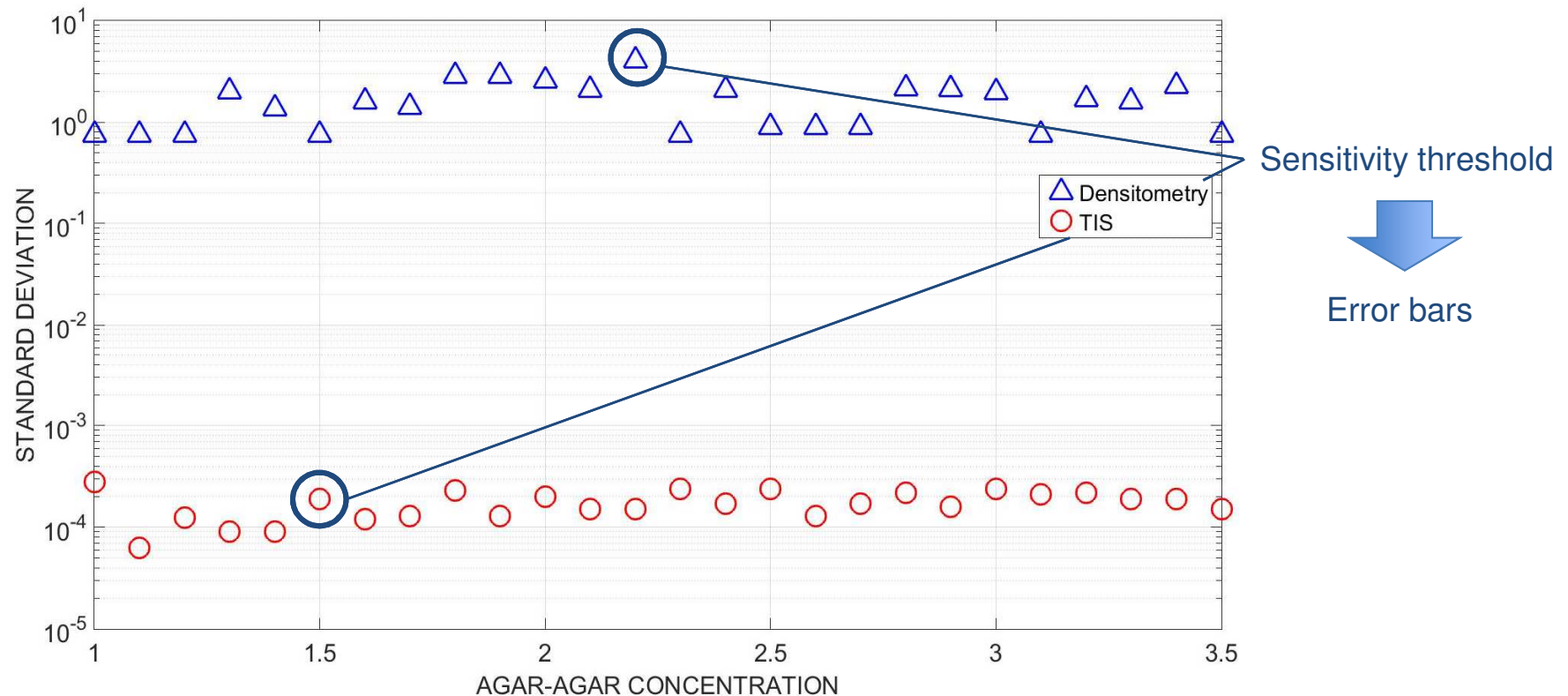
≈ 4 decades
Better repeatability with
the angular resolved
scattered intensity than
with the Pentacam®.

Performance of the method and comparison

Sensitivity threshold



- Definition: minimal threshold between two measurements to consider them as different
- The maximal standard deviation obtained is defined as the sensitivity threshold



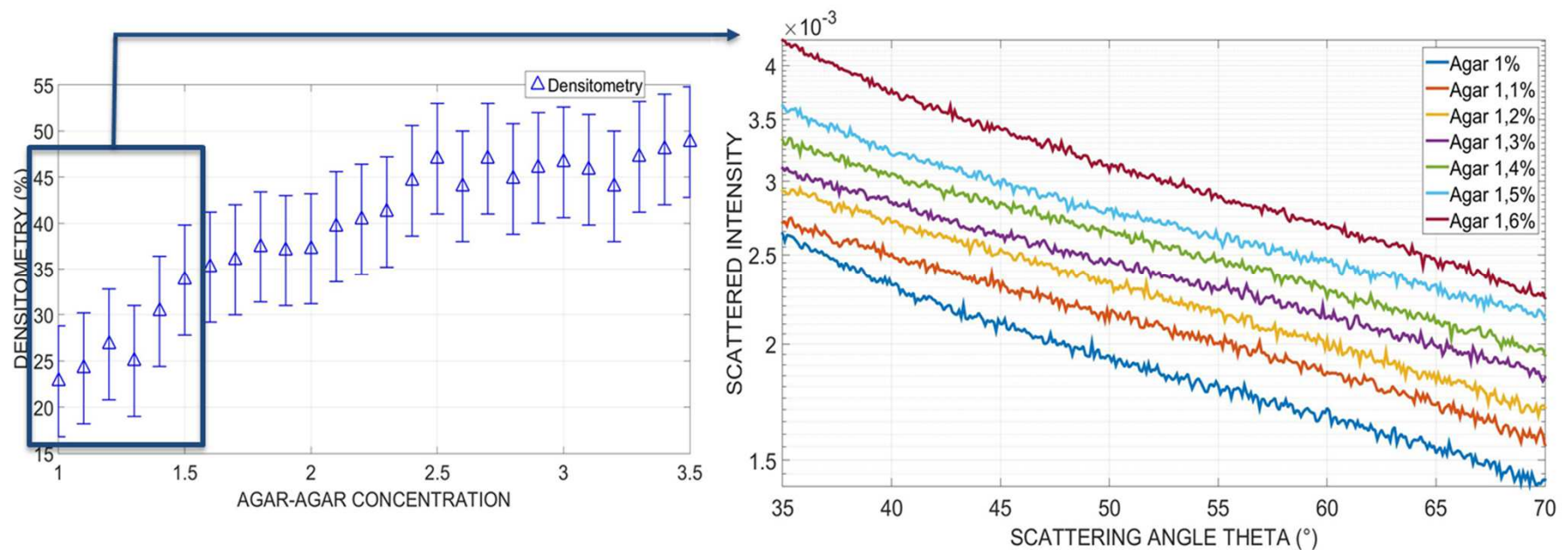
Performance of the method and comparison


Comparison of the sensitivity to a variation of transparency

Comparison

Agar-Agar samples

- Angular-resolved scattered light intensity measurements are more sensitive to a variation of transparency than the Pentacam®
- The access to large angles increase the sensitivity



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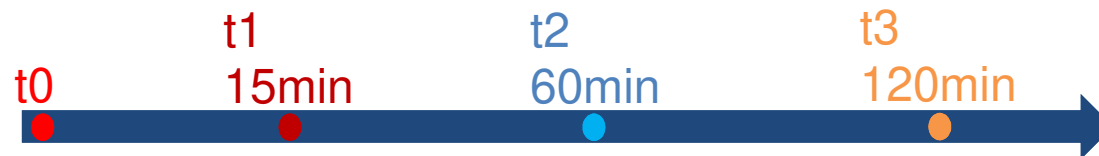
Application to corneal grafts

Comparison of the sensitivity to a variation of transparency

Corneal grafts

- Tissue rejected from the Eye Tissue Bank of EFS Marseille
- Variation of the thickness and of the transparency:

Induction of an edema in soaking them in an hypo osmolar solution



Measurements

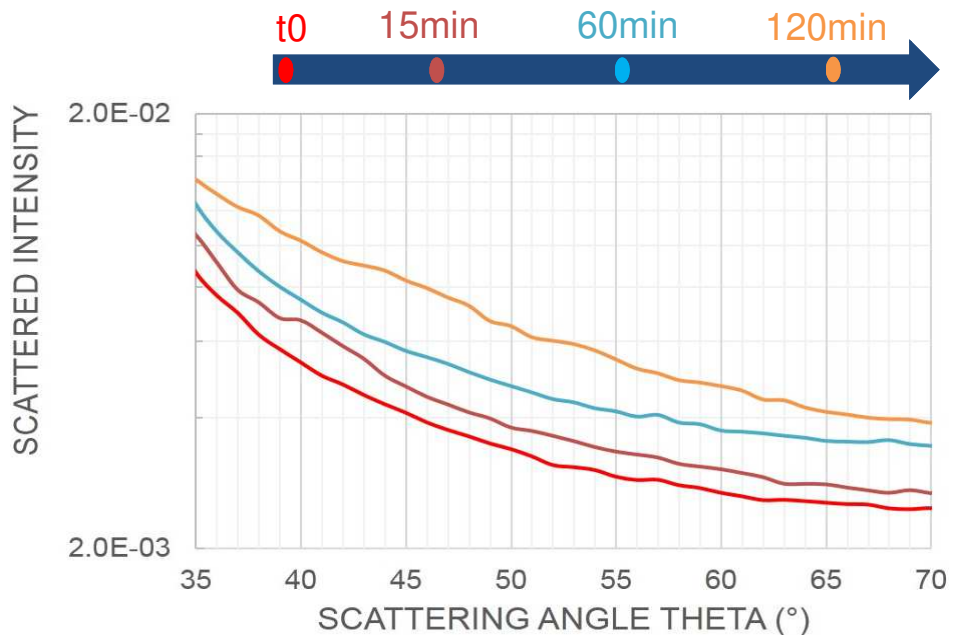
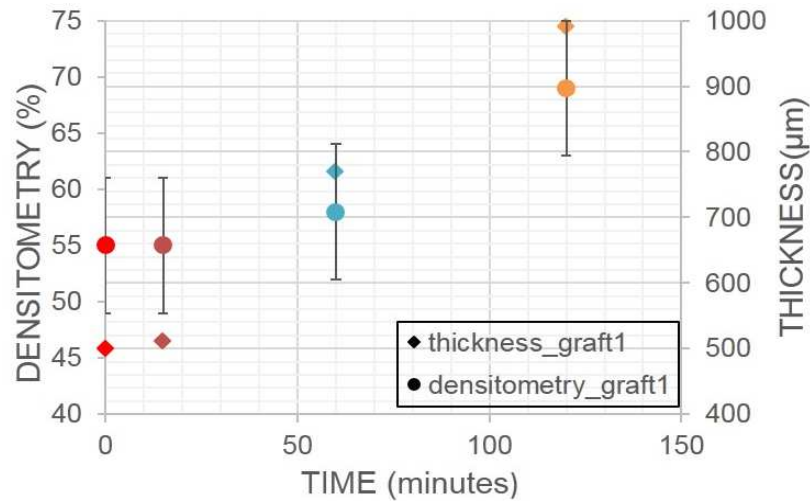
- Thickness (OCT)
- Densitometry (Pentacam®)
- Backscattered light (Proposed tool)

Application to corneal grafts

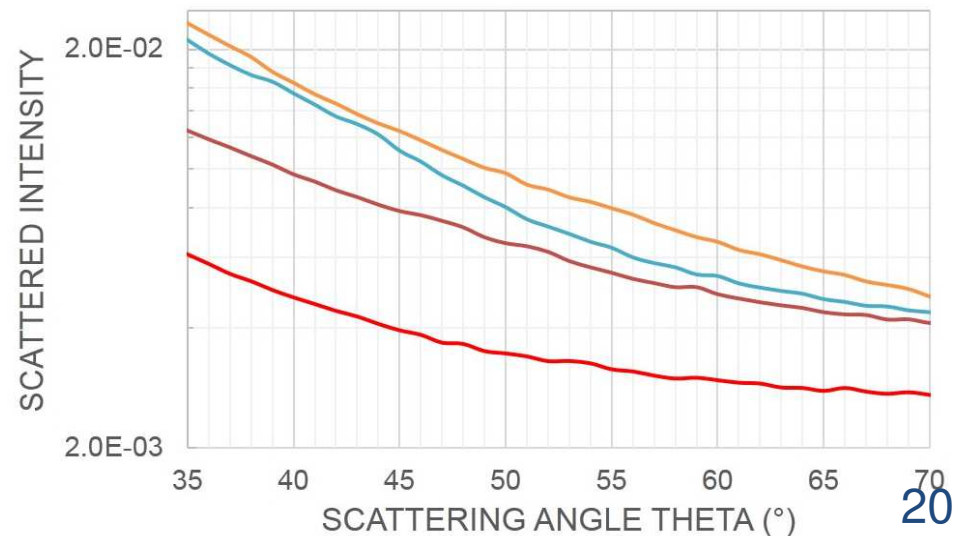
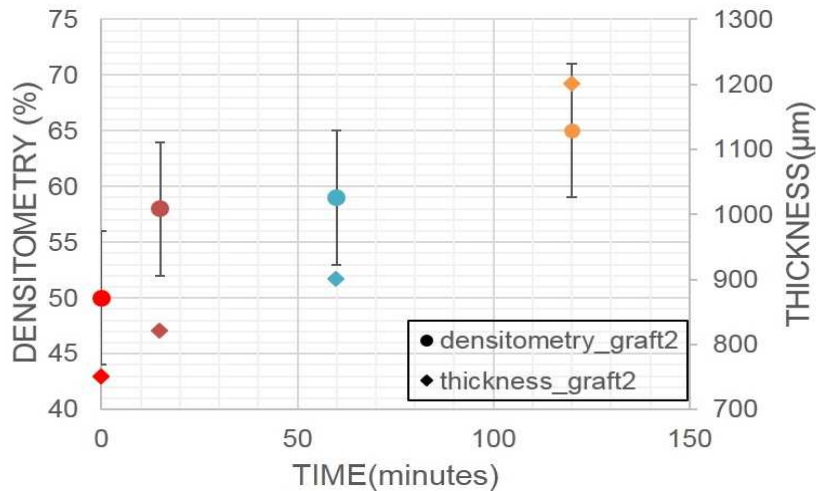
Comparison of the sensitivity to a variation of transparency


Corneal grafts

Graft 1



Graft 2



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Conclusion and perspectives

Conclusion

- The proposed method has a better repeatability and sensitivity
- Access to smaller scale and permit to select the bulk scattering
- Precocious diagnosis of a loss transparency

Perspectives

- Study of the influence of the different structure scale on the scattering (numerical simulations)
- In vivo diagnosis



Assistance Publique
Hôpitaux de Marseille



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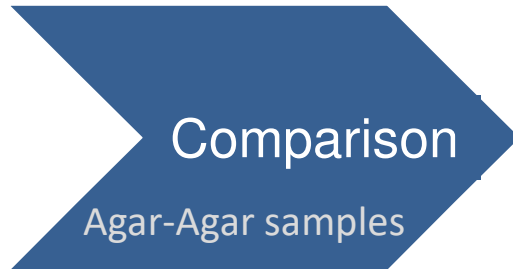
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