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UFO (Unidentified Full Objects) Sighted in The Cornea: Can We Make The Diagnosis By Means of *in vivo* Confocal Microscopy?

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Introduction

In vivo confocal microscopy (IVCM) is a powerful diagnostic technique that provides minimally invasive, high resolution, steady-state assessment of the corneal cellular structure [1]. Rapid scanning is used to recreate a full field of view and to get a ''real time'' viewing [2] Because of its ability to analyze living tissue at cellular levels, IVCM represents a valid tool for clinical diagnosis and management of corneal diseases [3]. It may be useful in the areas of infective keratitis, corneal dystrophies, refractive surgery, and contact lens wear, where it allows for differential diagnosis and detection of subtle short and long-term changes [2]. In our study, we evaluate the efficacy of IVCM in the diagnosis of corneal disease.

Materials and Methods

Thirty eyes of 30 patients with corneal diseases were included in the study. All patients underwent IVCM and color picture of the anterior segment. A color photograph of the entire ocular surface of each eye was obtained using a slit lamp and Ekta chrome, 16x magnification.

Heidelberg Retinal Tomograph with Rostock Corneal Module (HRT-RCM) (Heidelberg Engineering, GmBH, Dossenheim, Germany) was used to evaluate the corneal structure. The system design and use of this confocal microscope have been described in detail [4]. Before the examination, a drop of a topicalanesthetic, proparacaine hydro chloride ophthalmic solutionof 0.5%, was administered to the cornea, and a drop of 2.5% hydroxyl propyl methyl cellulose was placed at the tip of the objective to serve as an immersion fluid. The patient was asked to focus on a fixation device to allow for the alignment of the objective to the region of interest. Sections of the peripheral and central cornea were imaged. Real-time images of all layers of the cornea were detected through the use of a low-light camera and recorded. The images were digitized and stored in computer memory.

Round hyper-reflective bodies seen with *in vivo* confocal microscopy were defined as UFOs (Unidentified Full Objects). Frames containing UFOs were selected and analyzed by a masked observer (MP), to ascertain whether confocal images alone were sufficient to formulate a correct diagnosis. The masked observer was then provided with the color picture of the cornea and asked to re-assess his/her previous diagnosis if needed.

Results

Fifteen out of the 30 patients presented Acanthamoeba keratitis (AK); 4 conjunctival pigmented lesion; 3 Map-Dot-Fingerprint keratopathy; 3 post-LASIK Diffuse Lamellar Keratitis (DLK); 2 fungal keratitis; 2 epithelial in-growth and 1 corneal pigmented lesion. *In vivo* confocal microscopy allowed for correct diagnoses in 22 cases (73%), whereas in 8 the diagnosis was incorrect. Patients with AK and fungal keratitis were correctly diagnosed. DLK patients were generically diagnosed as having "corneal scarring" and subsequently correctly diagnosed through examining the color picture. Out of the 8 misdiagnosed cases, 7 were correctly diagnosed once the color picture of

the cornea was provided. One patient affected by Map-Dot-fingerprint was misdiagnosed as suffering from AK even after examining the color picture (Table 1) (Figure 1 & 2).

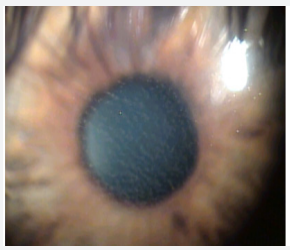
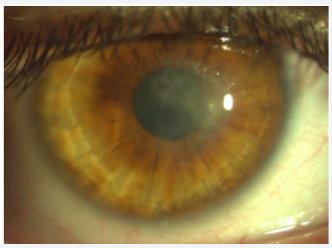

Figure 1

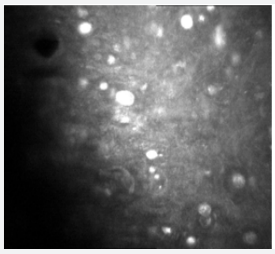
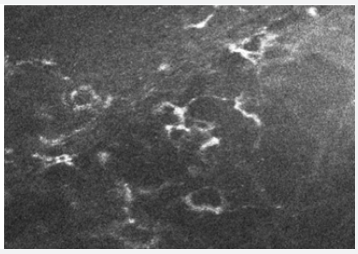

Figure 2

Table1:

Diagnosis	Diagnosis with Confocol Micropsy	Diagnosis with Confocol Micropsy and Color Picture
15 patients: Acanthamoeba	15 patients: Acanthamoeba keratitis	15 patients: Acanthamoeba keratitis
4 Patients: conjunctival pigment lesions	3 Patients: fungal keratitis 1 Patient: Conjuctival pigmented lesion	4 patients: Conjuctival pigmented leisons
3 patients: Map-Dot-finger print distrophy	2 patients: Map-Dot finger print distrophy 1 patient: Acanthamoeba keratitis	2 patients: Map-Dot-finger print distrophy 1 patient: Acanthamoeba keratitis
3 patients DLK	3 Patients corneal scarring	3 patients DLK
2 Patients: fungal keratitis	1 patient: pigmented lesion of the cornea 1 patient fungal keratitis	2 patients: fungal keratitis
2 Patients: fungal keratitis	1 patient: epithelial ingrowth 1 patient: fungal keratitis	2patients: epithelial in growth
1 patient:corneal pigmented lesion	1 patient: corneal pigmented lesion	1 patient: corneal pigmented lesion
1 patient: ocular cicatrical pemphigoid	1 patient: pigmented lesion	1 patient: ocular cicatrical pemphigoid

Conclusion

In vivo confocal microscopy is a non-invasive examination that provides relevant information on corneal anatomy [5] Its role in the clinical setting has been the most described in the management of infectious keratitis [6]. Even if corneal scraping and biopsy remain the gold standard in the micro biology diagnosis, IVCM may facilitate early diagnosis and the initiation of targeted antimicrobial therapy. It is particularly valuable in challenging cases such as contactlens- related AK [7]. Acanthamoebacysts, trophozoites and fungal hyphae can be identified by using IVCM directly [8]. In a prospective, double-masked, observational study [9], the sensitivity of IVCM in recognition of Acanthamoebacysts and fungal elements was 88.3%, and specificity was 91.1%. As previously stated by the American Academy of Ophthalmology which reported level II evidence for the adjunctive role of IVCM in the diagnosis of AK [6,10]. Nevertheless, clinical pictures are instrumental in getting the correct diagnosis. In our study, UFOs were mostly mis interpreted as Acanthamoeba cysts, probably because that they are easily identified by this tool thereby yielding a high rate of false positive findings. One single image of IVCMis deemed insufficient if correct diagnoses are to be made, as findings may well overlap in different diseases. Nevertheless, when integrated with bio-microscopic findings, this tool is essential if prompt, accurate and non-invasive diagnoses of corneal disease are to be formulated.

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