In vivo volumetric imaging of the human upper eyelid with ultrahigh-resolution optical coherence tomography

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Abstract. The upper eyelid is a biological tissue with complex structure, essential for the maintenance of an optically clear ocular surface due to its physical (blinking) effect. The Meibomian glands (MGs) are structures that lie beneath the surface of the inner eyelid and are partially responsible for the production of the superficial oily layer of the tear film. The MGs are only superficially visible under magnification when the eyelid is everted. We present for the first time in vivo 3-D images of healthy and inflamed human MGs. Tomograms were acquired from the tarsal plate of everted human eyelids with a 1060-nm ultrahigh-resolution optical coherence tomography (UHOCT) system, with \( \sim 3 \mu m \times 10 \mu m \) (axial \times\) lateral resolution in biological tissue at the rate of 91,911 A-scans/s. Comparison with histology shows that the UHOCT images reveal a spatial distribution of structures that appear to correspond with the MGs' acini and ducts (in healthy subjects), and accumulation of heterogeneous, highly scattering biological material and clear fluids in the visibly blocked glands. Noninvasive, volumetric high-resolution morphological imaging of the human tarsal area could have a significant impact in the clinical diagnosis of inflammatory and noninflammatory lid pathologies. © 2010 Society of Photo-Optical Instrumentation Engineers. [DOI: 10.1117/1.3475957]

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The human upper eyelid has two principal roles: it acts as a protective barrier for the globe, closing the eye in response to prevent any potential penetration of a foreign body, and it also has a lubricating mechanism whereby the tear film covering the anterior surface of the eye is replenished by routine involuntary blinking. Located in the upper eyelid and super-
the everted eyelids of three human subjects. The imaging procedure was approved by the University of Waterloo Human Ethics Committee. Two of the subjects had normal, healthy eyelids, while the third had an inflamed MG (chalazion). The subjects were prescreened and their eyelids everted by a licensed optometrist. Volumetric images (1000 × 512 × 256), corresponding to 4-mm × 1 mm × 2 mm physical dimensions (horizontal × depth × vertical), were acquired from different locations in the eyelid, in direction from the fold toward the marginal area, perpendicular to the tissue surface and across the orientation of the MG’s main ducts.

Figure 1 shows representative UHROCT 2-D images [(b) and (c)] of a healthy human eyelid. For comparative purposes, a representative upper eyelid histology (periodic acid Schiff (PAS) staining) image is also shown (a). The UHROCT 2-D images were obtained perpendicular to the known anatomic course of the MG’s main ducts, as illustrated by the black line on the histology image [Fig. 1(a)]. The UHROCT image dimensions were 1000 × 400 (A-scans × pixels), corresponding to 4-mm lateral and ~0.8-mm depth scan. The tomograms show relatively homogeneous superficial tissue presumably, the inner surface connective tissue of the tarsal plate [Fig. 1(b) black arrow] and a network of low-reflective lobes with connecting ducts presumably cross sections of the MG acini [Fig. 1(c) white arrow] and ductules [Fig. 1(b) white arrow] adjacent to an additional area of relatively homogeneous tissue (presumably, outer surface connective tissue of the tarsal plate).

Two videos, presented in Fig. 2, show a cross-sectional view (a) and an en face view (b) of a representative volumetric image set of the human upper eyelid. The image sequence in Fig. 2(a) was acquired in the direction from the fold of the everted eyelid toward the eyelashes and exhibits cross sections of ductlike structures (low-reflective, dark brown, large circular features) and associated smaller irregularly shaped lobes (pale brown). The video in Fig. 2(b) shows the same structures in en face view. The lobelike structures appear to form clusters near the ends of the ductlike structures, leading us to conclude that they likely correspond to the MG’s acini and ductules, respectively, as seen in histological observations of the eyelid structure. The ductlike structures appear similar to large blood vessels, although there are major differences: the cross section of an MG’s main duct increases in direction from the fold toward the eyelashes, and the main ducts of all MGs in the human eyelid are oriented parallel to each other, which corresponds to the morphological features observed in the en face tomograms [Fig. 2(b)].

Figure 3 shows a selection of representative en face images from the video in Fig. 2(b). The tomogram shown in Fig. 3(a) was acquired ~200 µm below the tissue surface, and there appears to be a large, ductlike structure [presumably the MG main duct; Fig. 3(b) black arrow]. To the temporo-lateral (right) side, there appears to be additional duct structure that is positioned deeper from the inner surface of the eyelid. On the naso-lateral (left) side of the large ductlike structure, a cluster of low-reflective (pale brown), irregularly shaped lobular features (presumably acini) appears, visible on the highly reflective background. A magnified (2 ×) view of the section in Fig. 3(a) marked with the white rectangle is shown in Fig. 3(b), where the lobular features are better observed. The sequence of en face images [Figs. 3(c), 3(d)] obtained from different depths within the everted eyelid shows the spatial distribution of the ductlike and lobular features within the tissue.

Volumetric images were also acquired from a clinically diagnosed chalazion (nodular swelling in the tarsal plate), and representative tomograms are shown in Fig. 4. The images were acquired in the direction from the fold of the everted eyelid, across the visible, superficial mass of the chalazion, toward the eyelashes. Figure 4(a) shows the structural appearance of the relatively unaffected tissue adjacent to the mass of the chalazion. In Fig. 4(b), a small region of highly reflective tissue, enveloped in a thin membrane and surrounded by optically clear material (likely fluid; black arrow) is visible. Figure 4(c) shows a cystlike feature of almost round shape, with a thick membrane [Figs. 4(c) and 4(d) black arrow], filled with optically clear material, most likely fluid. The subsequent UHROCT tomograms acquired across the bulk of the swelling [Figs. 4(d–f)] show that as the size of the mass increases, its shape becomes more irregular and it is filled with clusters of highly reflective material [Fig. 4(d) gray arrow]. On the basis of current knowledge of the histopathological mechanisms associated with this type of swelling, the
observed highly reflective spots within the cyst may be agglomerations of inflammatory cells such as lymphocytes, epitheloid cells, or multinucleated giant cells, while the clear fluid may be liberated sebaceous material.

In summary, a state-of-the-art, high-speed, UHROCT system was used to acquire for the first time in vivo volumetric images of the everted human upper eyelid. The 3-D tomograms revealed the apparent intricate structure of the healthy Meibomian glands’ ducts and acini, which were previously seen only with ex vivo histological analysis. This work also demonstrates the clinical relevance and potential of the UHOCt technology for noninvasive diagnostics of abnormalities in the upper eyelid, by revealing the internal structure of a chalazion, something previously requiring a biopsy.

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References