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MISCELLANEOUS

Characteristics of lacrimal passage diseases by 80-MHz ultrasound biomicroscopy: an observational study

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Abstract

Purpose To investigate the microstructure of the lacrimal canaliculus and the characteristics of lacrimal canalicular diseases by 80-MHz ultrasound biomicroscopy (UBM).

Methods This study included 33 participants: 20 normal subjects (40 eyes), 2 patients with chronic lacrimal canaliculitis (4 eyes), 10 patients with chronic dacryocystitis (16 eyes), and 1 patient with lacrimal punctum atresia (2 eyes). All participants underwent 80-MHz UBM; disease-specific features were noted.

Results On 80-MHz UBM of the lacrimal canaliculi (vertical section) in normal subjects, low echo of the lacrimal canalicular lumen and high echo of the lacrimal canalicular wall were observed. The uniform low echo near the wall was the mucosal epithelium. The outermost layer of medium-to-high echo was the subepithelial elastic fibrous layer. In the horizontal section, the lumen was continuous. Two linear high echoes parallel to the canalicular wall could be observed at the center of the lacrimal canaliculus, which were sometimes attached and sometimes separated. When separated, the center of the lacrimal canaliculus was a low echo area (lumen). Lacrimal canaliculitis (vertical section) showed obvious ectasia of the lacrimal canalicular lumen, with a high echo mass shadow, which might have been calculi, and uneven thickness of the mucosal epithelium with a slightly high echo shadow. In the horizontal section, the lumen varied in size with clear boundaries of medium and high echoes. The central linear high echoes of the lumen were absent, and the echoes of the mucosal epithelium were discontinuous. In chronic dacryocystitis, the lacrimal canalicular lumen was extensively enlarged, with continuous echoes and uniform thickness of the mucosal epithelium and homogeneous patches of slightly higher echoes. Lacrimal punctum atresia indicated that the lacrimal canaliculus existed in both eyes and its structure was normal.

Conclusions The 80-MHz UBM is a new non-invasive technique that can be used for clear visualization of the fine structure of the lacrimal canaliculus, including the mucosal epithelium and subepithelial elastic fiber layer. The use of this approach will improve understanding of the hierarchical structure of the lacrimal canaliculi and provide a comprehensive basis for diagnosis, differential diagnosis, and treatment plan in patients with lacrimal passage diseases.

Keywords 80-MHz ultrasound biomicroscopy · Dacryoendoscopy · Lacrimal canaliculus · Lacrimal canaliculitis

Introduction

Lacrimal canalicular diseases are common conditions that involve the lacrimal passage. However, some forms of lacrimal canalicular diseases are easily misdiagnosed (e.g., lacrimal canaliculitis is often misdiagnosed as chronic dacryocystitis). Additionally, in the clinical setting, it is often unclear whether the structure of the lacrimal canaliculus is normal in patients with lacrimal punctum occlusion.

In recent years, researchers have focused on the dynamic mechanism of the lacrimal passage, especially the physiological state of the lacrimal canaliculi (e.g., whether the lacrimal canaliculi are open or closed). In order to explore these aspects, more effective examination methods are needed to elucidate the status of the lacrimal canaliculi. It is particularly important to identify an imaging method that can clearly show the status of the lacrimal canaliculi. Since lacrimal canaliculi

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have a superficial position and a fine structure, it is difficult to clearly display the structure of the lacrimal canaliculi by normal imaging modalities such as computed tomography dacryocystography (CTD) and magnetic resonance dacryocystography (MRD). Dacryoendoscopy is quite convenient for the examination of lacrimal canalicular diseases. However, the condition of the lacrimal canaliculus in patients with lacrimal punctum atresia remains uncertain, and this examination causes a certain traumatic effect on the lacrimal canaliculus. Further, ultrasound biomicroscopy (UBM) is a non-invasive examination and provides high resolution; owing to these factors, it is expected to be an ideal method for examining the lacrimal canaliculus.

UBM was first used as a diagnostic tool in ophthalmology in 1956 [1]. With the development of in vivo and real-time observation technology, the ultrasonic frequency increased, and the image resolution improved. UBM can display the cornea, anterior chamber, ciliary body, lens zonule, lens, and anterior choroid, as well as other fine structures of the eye, such as the lacrimal passage [2–6]. Previous studies have used 50-MHz UBM and modified the swimming goggle that serves as an eyecup to observe the lacrimal passage, which can show the structure of the lacrimal system [6]. Although 50-MHz UBM can be used to visualize the lacrimal system, the final image might be missing some information because of the limited resolution and requirement of the modified swimming goggle as a medium. The 80-MHz UBM has a higher resolution compared with the 50-MHz UBM and does not require swimming goggles as a medium, as it can directly be in contact with the skin surface or conjunctival surface for examination [7]. Therefore, the attenuation of ultrasound would be smaller, imaging quality would be better, and details would be clearer with 80-MHz UBM than with 50-MHz UBM. The 80-MHz UBM can show details that the 50-MHz UBM cannot display [7]. Thus, 80-MHz UBM could enable clinicians to observe the lacrimal canaliculi more accurately in vivo and to examine their structure in better detail.

The 80-MHz UBM is a non-invasive examination. Thus, it is more acceptable for patients in terms of comfort and does not damage the lacrimal passage [7]. The 80-MHz UBM examination is not only economic, convenient, and non-invasive, but also has the advantages of high resolution and fine structure display [7]. Our team used 80-MHz UBM to study Schlemm's canal; its diameter and cross-sectional area were measured and recorded [8, 9]. Considering that 80-MHz UBM can clearly show such fine structures as Schlemm's canal, we believe that it can also display the lacrimal canaliculi more clearly and in greater detail compared with 50-MHz UBM. In this study, we aimed to describe the microstructure of the lacrimal canaliculus and investigate the characteristics of lacrimal canalicular diseases by using 80-MHz UBM.

Materials and methods

The ethics committee of Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, approved this observational study, which adhered to the tenets of the Declaration of Helsinki. All subjects provided written informed consent before study participation.

Subjects

Thirty-three participants were recruited, including 20 normal subjects (40 eyes), 2 patients with lacrimal canaliculitis (4 eyes), 10 patients with chronic dacryocystitis (16 eyes), and 1 patient with lacrimal punctum atresia (2 eyes). Patients with ocular diseases (except for lacrimal passage diseases) or surgery, which might have an influence on the morphology of canaliculus, would be excluded from this study (e.g., blepharitis, conjunctivitis, conjunctival tumors, eyelid tumors, inner canthus tumors, blepharoplasty, etc.). Subjects younger than 18 years old were also excluded. All participants underwent 80-MHz UBM examination, the fluorescein dye disappearance test (DDT), and lacrimal irrigation. Patients with lacrimal canaliculitis also underwent dacryoendoscopy.

Fluorescein dye disappearance test

Fluorescent dye was dropped on the conjunctival sac. The results of the DDT were recorded as follows: positive (if the dye disappeared or if there was faint dye in the tear film after 5 min), delayed (if the dye partially disappeared after 5 min or there was a lightly stained conjunctival cul-de-sac after 10–15 min), or negative (if there was a thick meniscus of fluorescein-tinted tears with a deeply stained conjunctival cul-de-sac after 5 min).

Imaging of the lacrimal passage

We examined subjects using an 80-MHz UBM imaging system (iUltrasound; iScience Interventional, Inc., Menlo Park, CA). Images were obtained using the following settings: transducer frequency, 80 MHz; axial resolution, 25 mm; lateral resolution, 50 mm; electronic resolution, 10 mm; tissue penetration depth, 2 mm; scan rate, 7 frames/s; and imaging window size, 4.0 × 4.0 mm. Before recording the iUltrasound measurements, the eyes were anesthetized with topical proparacaine hydrochloride eye drops, and a low-viscosity ultrasound gel was placed on the skin surface at the lacrimal punctum. The iUltrasound probe was directly placed on the skin surface at the lacrimal punctum, and the images were obtained in the vertical and horizontal sections.

Dacryoendoscopy

We examined patients with lacrimal canaliculitis using a dacryoendoscopy system (Endognost LS200, Polydiagnost GmbH, Munich, Germany). After nerve block anesthesia was performed, the probe of the dacryoendoscope (diameter, 1.1 mm) was inserted after dilating the lacrimal puncta, and it entered the lacrimal sac along the direction of the lacrimal canaliculus. After positioning the probe, it was placed vertically against the bone wall, rotated downward, and then inserted into the nasolacrimal duct and subsequently into the nasal cavity. The images were recorded during this process.

Results

Normal subjects

Twenty participants (40 eyes, 40 lacrimal canaliculi)

Normal subjects' DDT results were negative. Both the superior and inferior lacrimal passages were unobstructed. In terms of the 80-MHz UBM, the horizontal-sectional image of the lacrimal canaliculus showed a low echo for the lacrimal canalicular lumen and a high echo for the lacrimal canalicular wall. The uniform low echo near the wall was the mucosal epithelium. The outermost layer of the medium to high echo was the subepithelial elastic fibrous layer. These structures were consistent with the pathological results (Fig. 1).

In the vertical section, the lumen was continuous. The normal human lacrimal canaliculus was not always open in the 80-MHz UBM images. Two linear high echoes parallel to the wall of the canaliculus could be seen at the center of the lacrimal canaliculus, which were sometimes attached and sometimes separated. When separated, the center of the lacrimal canaliculus appeared as a low echo area (lumen) (Fig. 2). In addition, the superior lacrimal canaliculus, end of the inferior lacrimal canaliculus, and lacrimal canalidull were also observed in one of the study subjects (Fig. 3).

Lacrimal canaliculitis

Two patients (4 eyes, 8 lacrimal canaliculi)

One patient had chronic superior lacrimal canaliculitis. The DDT results were recorded as positive. Both the superior and inferior lacrimal passages were unobstructed (Fig. 4). The 80-MHz UBM (horizontal section) showed obvious ectasia of the upper lacrimal canalicular lumen, with a high echo mass shadow, which might have been calculi. Additionally, it showed uneven thickness of the mucosal epithelium, with a slightly high echo shadow. In the vertical section, the lumen had different sizes and clear boundaries of medium and high echoes; central linear high echoes of the lumen were absent, and echoes of the mucosal epithelium were discontinuous. The structure of the inferior lacrimal canaliculi was normal in both eyes.

Dacryoendoscopy of the lacrimal canaliculus showed that the superior lacrimal canalicular lumen was enlarged and the mucosa was red and white with a large number of inflammatory manifestations such as membranous exudation and calculi, while endoscopy of the inferior lacrimal canaliculi showed a smooth wall without inflammatory manifestations, such as calculi (Fig. 5). Another patient had acute inferior lacrimal canaliculitis. The DDT result was recorded as positive. The inferior lacrimal passages were unobstructed, and secretions could be seen rushing out from the inferior lacrimal passage. The 80-MHz UBM (horizontal section) showed obvious ectasia of the inferior lacrimal canalicular lumen, with a high echo mass shadow, which might have been calculi. It also showed uneven thickness of the mucosal epithelium with a slightly high echo shadow that may have been inflammatory secretion. Dacryoendoscopy of the lacrimal canaliculus showed that the inferior lacrimal canalicular lumen was

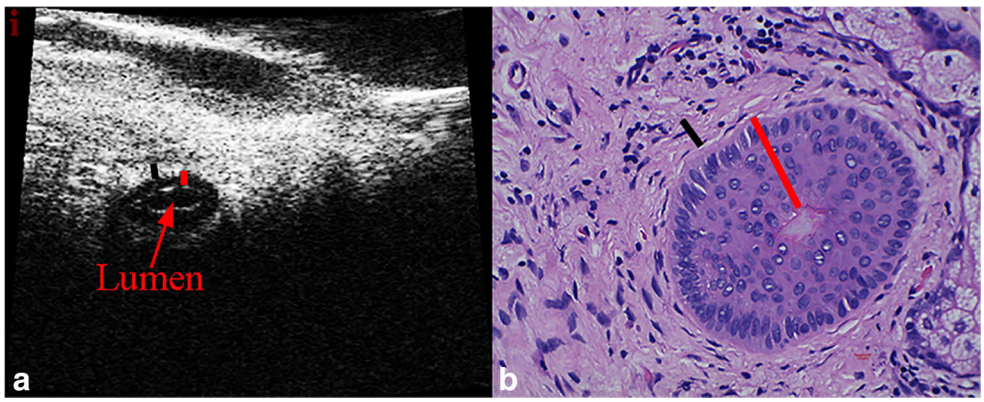

Fig. 1 80-MHz UBM image (horizontal-section) and pathological slice of normal lacrimal canaliculus. **a** Lumen, low echo (white arrow); lacrimal canalicular wall, high echo. The uniform low echo closed the wall was mucosal epithelium (red line). The outermost layer of medium-to-high echo was subepithelial elastic fibrous layer (black line). **b** The pathological slice of normal lacrimal canaliculus

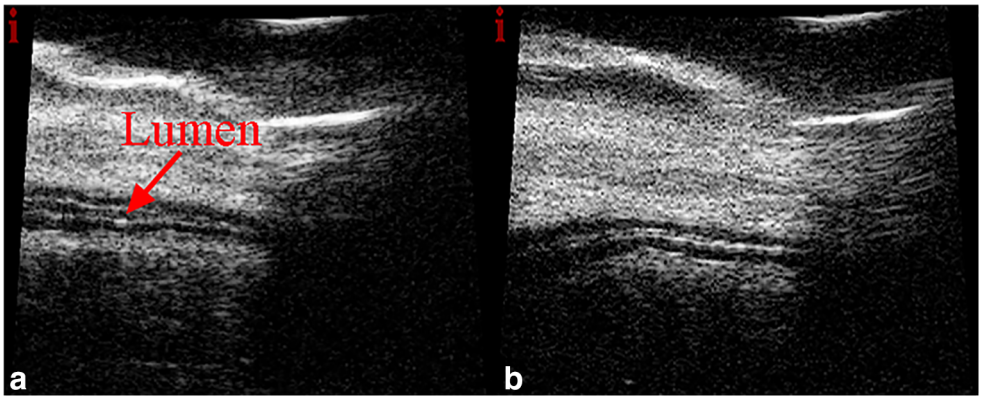

Fig. 2 80-MHz UBM image of normal lacrimal canaliculus. **a** Two linear high echoes parallel to the wall of canaliculus could be seen in the center of lacrimal canaliculus. Sometimes separated from each other. When separated, the center of lacrimal canaliculus was a low echo area (red line).**b** Sometimes attached to each other

enlarged and the mucosa was red and white with a large number of inflammatory manifestations, such as membranous exudation and calculi. The patient underwent lacrimal canaliculotomy plus calculi removal. Three days later, the symptoms of epiphora were remarkably relieved, and the 80-MHz UBM showed that inflammation of the inferior lacrimal canaliculus had markedly improved (Fig. 6).

Chronic dacryocystitis

Ten patients (16 eyes, 32 lacrimal canaliculi)

The DDT results were recorded as positive. Both the superior and inferior lacrimal passages were obstructed. At the same time, mucopurulent secretion reflux was observed. The 80-MHz UBM showed that the lacrimal canalicular lumen was extensively enlarged, echoes of the mucosal epithelium were continuous, and the thickness of the mucosal epithelium was uniform, with homogeneous patches of slightly higher echoes. The slightly higher echo shadow might have been caused by the secretion of the lacrimal sac, which flowed back to the lacrimal canaliculus (Fig. 7).Compared with that in lacrimal canaliculitis, the lumen was more extensively enlarged; the thickness of the mucosal epithelium was uniform, and the echoes of the mucosal epithelium were continuous in patients with chronic dacryocystitis, while those of the mucosal epithelium were uneven and discontinuous in patients with lacrimal canaliculitis. This finding suggested that 80-MHz UBM of the lacrimal canaliculi could be used to differentially diagnose lacrimal passage disease.

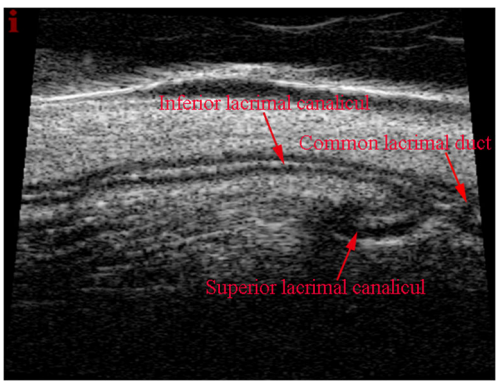

Fig. 3 The superior lacrimal canaliculus, the end of the inferior lacrimal canaliculus, and the lacrimal canalidull were also observed

Inferior lacrimal punctum atresia

One patient (2 eyes, 2 lacrimal canaliculi)

The DDT result was recorded as positive lacrimal irrigation, and the inferior lacrimal puncta was not found. The 80-MHz UBM showed that the inferior lacrimal canaliculus existed in both eyes and its structure was normal (Fig. 8). After lacrimal punctoplasty, the symptoms of epiphora were markedly relieved.

Discussion

Researchers have developed many imaging examinations to elucidate the structure of the lacrimal passage in vivo, such as CTD, MRD, and dacryoendoscopy. However, these examinations have their limitations. The radiation of CTD is substantial, and MRD is expensive; these modalities are suitable for the examination of the lacrimal sac and nasolacrimal duct lesions, but poor choices for the lacrimal canaliculi. Dacryoendoscopy could show the lacrimal canaliculus, but it is an invasive examination, as it requires nerve block anesthesia and might cause damage to the lacrimal canaliculus. In addition, the technique cannot identify features such as a lacrimal canaliculus with congenital absence of the lacrimal puncta and an obstructed lacrimal canaliculus, as well as the relationship of these features to their surrounding tissues [10, 11]. Furthermore, patients experience discomfort during the

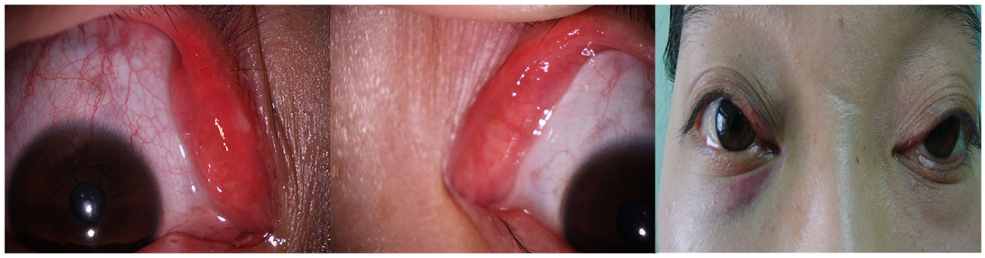

Fig. 4 The imaging of chronic superior lacrimal canaliculitis. The skin on the inside of the upper eyelid was red and swelling with slight valgus, eyelid conjunctival squamous metaplasia, the inside of the eyelid margin cover the pupil about 1 mm, eyelid relaxation. The superior lacrimal punctum was not visible. The form of the inferior lacrimal punctum is normal

examination. In order to overcome the disadvantages of these examinations, Pavlin et al. first applied UBM in lacrimal passage imaging diagnosis in the 1990s [12]. UBM as a noninvasive, safe, economical, and effective examination is favored by researchers. UBM has the characteristics of vivid imaging and could be used as an additional imaging examination for lacrimal canalicular diseases. Jeffrey et al. used 50-MHz UBM and modified swimming goggles to serve as an eyecup to observe the opening of the lacrimal canaliculi and the vertical and horizontal sections of the lacrimal canaliculi [13]. However, 50-MHz UBM cannot show the mucosal epithelium and subepithelial elastic fibrous layer, and the use of 50-MHz UBM may lead to misjudgment of the results (Fig. 9).

With further development of ultrasound technology, 80-MHz UBM with a higher resolution has emerged [7]. This instrument can provide clearer imaging and greater detail compared with 50-MHz UBM and can be in direct contact with the skin surface without the need for swimming goggles. Therefore, the imaging quality is higher, which promotes understanding of the lacrimal canalicular structure. The lacrimal canaliculi can also be observed in some cases. At the same time, we also observed that the lacrimal canaliculus did not remain consistently open, as it occasionally closed. This result indicated that the opening and closing of the lacrimal canaliculi may be rhythmic and the pressure of the lacrimal passage may be variable. The 80-MHz UBM can clearly show the structure of each layer of the lacrimal canaliculus, including the lumen, mucosal epithelium, and subepithelial elastic fibrous layer, which is consistent with the pathological results. Therefore, 80-MHz UBM enables ophthalmologists to observe the lacrimal canaliculi more accurately and to further elucidate the imaging structure of the lacrimal canaliculi. It can be used for the examination of various lacrimal diseases and the identification of lacrimal canaliculitis and chronic dacryocystitis. In the clinical setting, it is difficult to diagnose lacrimal canaliculitis, as it can be easily misdiagnosed as chronic dacryocystitis or conjunctivitis [14–16].

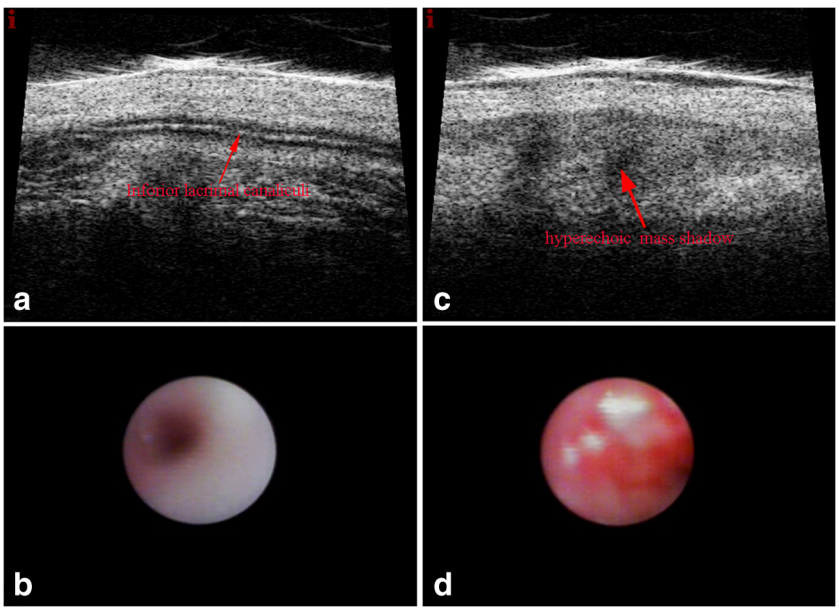

Fig. 5 80-MHz UBM and dacryoendoscopy images of superior lacrimal canaliculitis. **a**, **b** Normal lacrimal canaliculus. **c**, **d** Superior lacrimal canaliculitis. The cavity was enlarged and the hyperechoic mass shadowed in the center of the cavity. Dacryoendoscopy examination showed that the superior lacrimal canaliculus lumen was enlarged and the mucosa was red and white with a large number of inflammatory manifestations such as membranous exudation and calculi, while the inferior lacrimal canalicular endoscopy showed smooth wall without inflammation manifestations

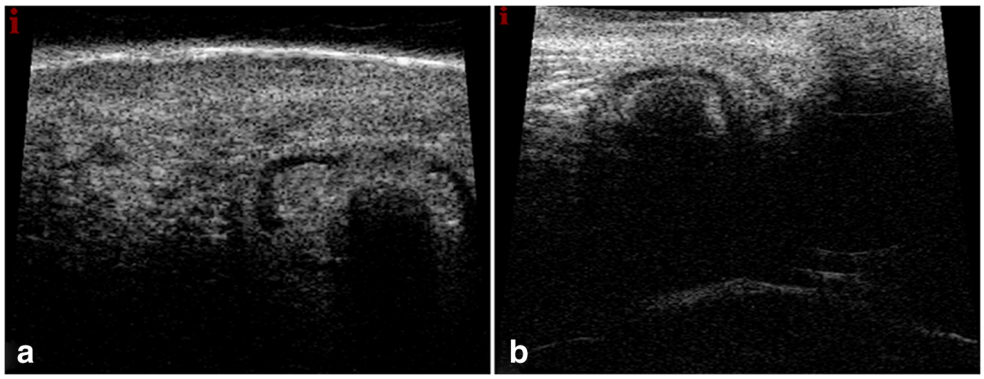

Fig. 6 80-MHz UBM images of inferior lacrimal canaliculitis before and after treatment. **a** Before treatment, **b** 3 days after treatment. The inflammation of inferior lacrimal canaliculus relieved significantly

The 80-MHz UBM can be used to non-invasively identify lacrimal canaliculitis and chronic dacryocystitis, avoiding misdiagnosis and inappropriate treatment. Only the lacrimal canalicular lumen of chronic dacryocystitis showed obvious enlargement; the thickness of the mucosal epithelium was still uniform, and no obvious inflammatory reaction was observed in the lacrimal canaliculus. However, the thickness of the mucosal epithelium in lacrimal canaliculitis was uneven. It was suggested that lacrimal sac inflammation was confined to the lacrimal sac and did not spread to the lacrimal canaliculus. The lacrimal canalicular mucosa might have certain resistance to the pathogenic bacteria of dacryocystitis. Moreover, our results suggested that the pathogenesis of lacrimal canaliculitis was different from that of dacryocystitis. In addition, 80-MHz UBM can be used to determine whether there are pathological changes in the lacrimal canaliculi and to provide a basis for the treatment strategy of lacrimal diseases. It can help ophthalmologists perform surgical procedures and evaluate prognosis in lacrimal punctum atresia.

In the past, because the condition of the lacrimal canaliculus was unknown, patients underwent intraoperative lacrimal canalicular exploration. However, exploration also causes trauma to the lacrimal canaliculus. Since the 80-MHz UBM can display the condition of the lacrimal canaliculi, unnecessary surgical procedures may be avoided and injury of the lacrimal canaliculi structure could be reduced. If the lacrimal canaliculi are normal, only lacrimal punctoplasty is needed during the operation.

This study had some limitations. The 80-MHz UBM technique had difficulty revealing the lacrimal duct, which was

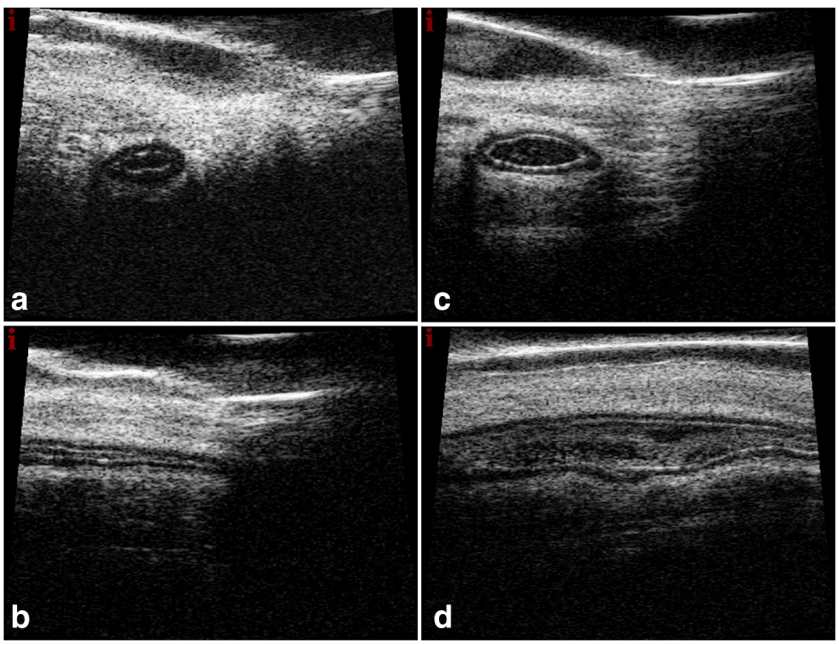

Fig. 7 80-MHz UBM images of chronic dacryocystitis. **a**, **b** Normal lacrimal canaliculus. **c**, **d** The lacrimal canaliculus of the chronic dacryocystitis was enlarged. The echoes of mucosal epithelium were continuous, and the thickness of the mucosal epithelium was uniform, with homogeneous patches of slightly higher echoes

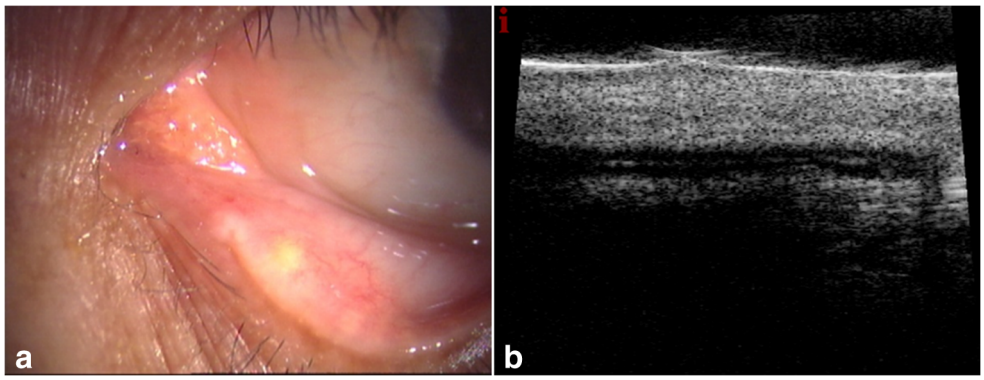

Fig. 8 The images of inferior lacrimal punctum atresia. Inferior lacrimal puncta was not found. 80-MHz UBM showed the inferior lacrimal canaliculus existed in both eyes and its structure was normal

observed only in one subject. This may have been due to the deep position of the lacrimal duct and the insufficient penetration of 80-MHz UBM. In addition, the lacrimal canaliculus was pulled occasionally during the procedure, thus changing its physiological state. Therefore, it is necessary to further improve this method for the measurement of the lacrimal canaliculus' physiological parameters.

Conclusions

The 80-MHz UBM can provide a more comprehensive basis for the diagnosis and differential diagnosis of lacrimal passage diseases. It can be used to diagnose lacrimal canaliculitis and chronic dacryocystitis and display the location and extent of lacrimal canalicular obstruction. Furthermore, 80-MHz UBM can display the status of the lacrimal canaliculi in patients with lacrimal punctum atresia and provide necessary information for ophthalmologists to decide whether to proceed with intervention of the lacrimal canaliculi during an operation of the lacrimal punctum. The 80-MHz UBM of the lacrimal canaliculi is a new non-invasive method that can clearly display the fine anatomical structure of the lacrimal canaliculus. It might be also used to perform quantitative measurements of the lacrimal drainage system, diagnose diseases, and evaluate the therapeutic effect. As a new non-invasive ophthalmic examination, 80-MHz UBM with a high resolution is expected to become the ideal clinical examination method for the lacrimal canaliculus.

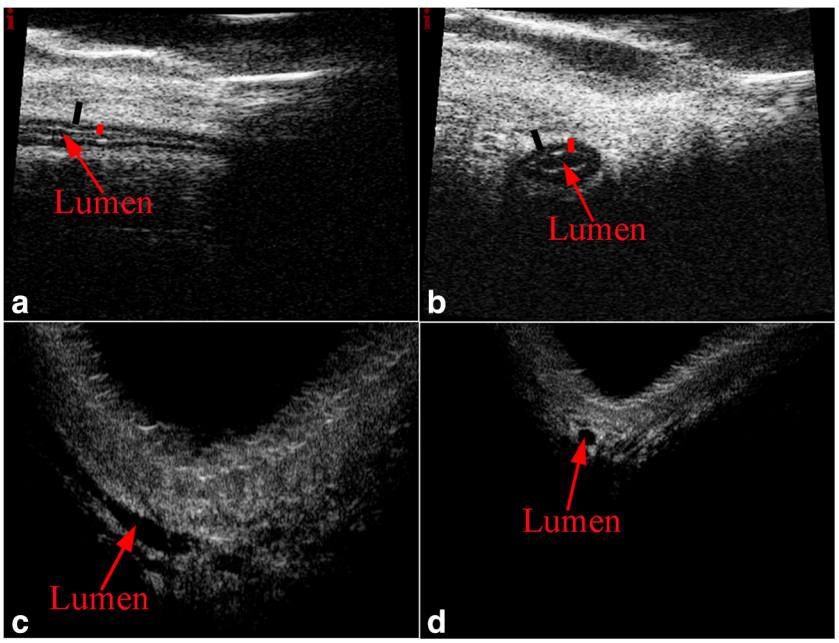

Fig. 9 Comparison of 80-MHz UBM image with 50 MHz UBM image of lacrimal canaliculus. **a**, **b** 80-MHz UBM imaging. Lumen, low echo (red arrow); lacrimal canalicular wall, high echo. The uniform low echo closed the wall was mucosal epithelium (red line). The outermost layer of medium to high echo was subepithelial elastic fibrous layer (black line). **c**, **d** 50-MHz UBM imaging

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the Tongji Hospital and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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