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Ultrasound Biomicroscopic Corneal Thickness Measurement for Corneal Thickness Mapping

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Abstract: Digitalized ultrasound biomicroscopic measurements of vertical cross sections from a 5 mm diameter area of the central cornea of normal and morbid eyes were used to create a computerized corneal thickness map. Mean corneal thickness in normal eyes was 0.503 ± 0.027 mm; the coefficient of variation, an index of reproducibility, was < 10% in all eyes. **Jpn J Ophthalmol 1997;41:12–18** © 1997 Japanese Ophthalmological Society

Key Words: Corneal thickness, corneal thickness mapping, ultrasound biomicroscopy.

Introduction

Corneal thickness is closely related to the functions of endothelial cells, making measurement of corneal thickness a helpful indicator when studying the pathophysiology of the cornea, and the endothelial cells, in particular.[1] There are currently three widely accepted methods for measuring corneal thickness: (1) the Haag-Streit pachometer (Hedby-Mishima method),[2] (2) ultrasound,[3,4] and (3) specular microscopy.[5] Pavlin et al[6,7] have recently reported on ultrasound biomicroscopic measurement (UBM) of corneal thickness. In this study, vertical cross-section images of a 5 mm diameter area of the central cornea were measured by UBM, and corneal thickness maps were created by computer from corneal thickness data.

Materials and Methods

Equipment

We used a Humphrey ultrasound biomicroscope (Model 840, Humphrey Instruments, San Leandro, CA, USA). Transducer specifications were: frequency, 50 MHz; focal distance, 5.5 mm; diameter, 3.0 mm; focal depth, 0.7 mm; resolution, 864 × 432 pixels per 5 × 5 mm; measurement resolution, ± 5 μm; mechanical linear scanning.

Received: February 6, 1996

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Part of this study was published in the Journal of the Japanese Ophthalmological Society 100:46-49 (1996).

Subjects

Twenty-two eyes of 15 healthy volunteers (ages: 25–62 years) who had no abnormalities, except ametropia, and did not wear contact lenses, were studied. Six morbid eyes (6 patients) were also studied: 2 from patients who had keratoconus; 2, corneal dystrophy; 1, corneal herpes; and 1, bullous keratopathy.

Methods

Thickness measurement. The subject was usually examined in a supine position looking up at the ceiling. For the scanning procedure, each subject received one drop of topical anesthetic (oxybuprocaine hydrochloride 0.4%, Benoxil®). The eyelids were held open by an eye cup and hydroxyethyl cellulose (Scopisol®) was poured into the cup. The subject focused his gaze on the ceiling during the procedure. With the transducer probe positioned perpendicularly to the cornea, and the distance adjusted so that the cornea was within the focal zone, scanning was done in the clock positions of 1:30 to 7:30, 3:00 to 9:00, 4:30 to 10:30, and 6:00 to 12:00. This provided a qualitative check on subject movement during the few minutes of scanning; 5 mm vertical cross-section images through a 5 mm diameter area of the optic center of the cornea were taken. Each image included the iris and the anterior part of the lens as well as the cornea. The point at which a line perpendicular to the tangent of the anterior surface of the lens crossed the corneal surface at the center of the pupil was regarded as the center of the cornea. Corneal thickness was measured with a scale on the monitor perpendic-

Published by Elsevier Science Inc.

0021-5155/97/$17.00
PII S0021-5155(96)00006-8

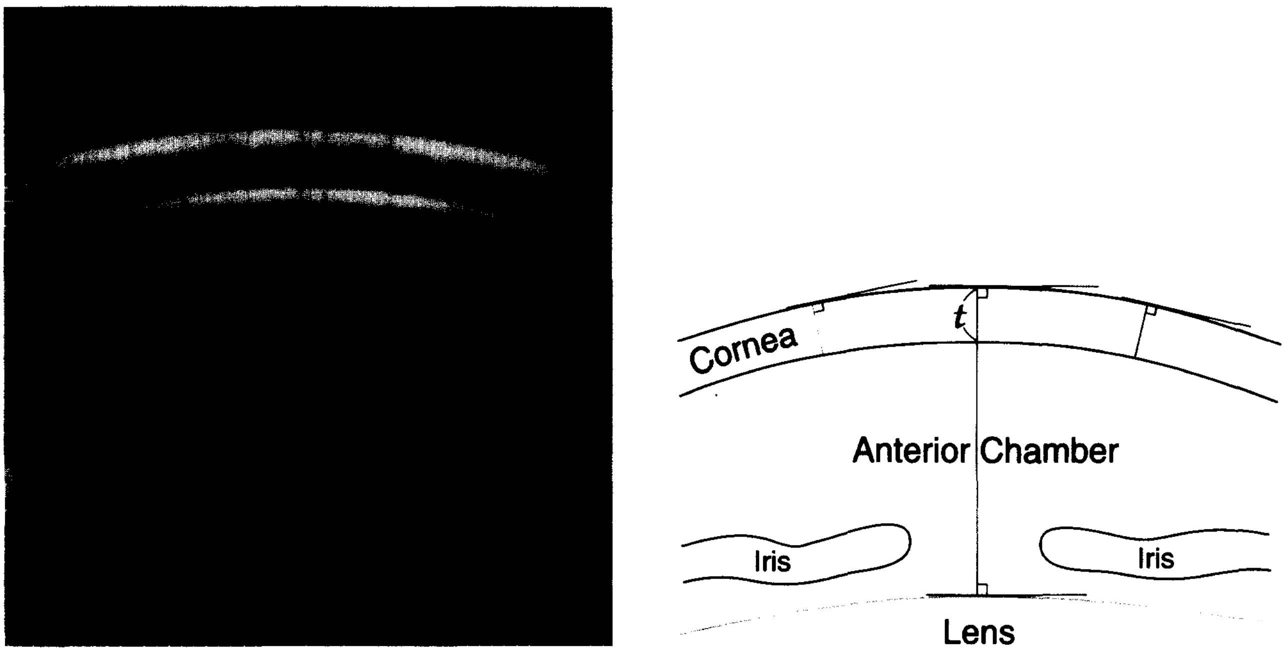

Figure 1. (**A**: left) Ultrasound biomicroscopic vertical cross section of the cornea. (**B**: right) Corneal center: the point at which a line perpendicular to the tangent of the anterior surface of the lens crosses the corneal surface in the center of the pupil. t = corneal thickness.

ular to the tangent of the corneal surface at 0.25 mm intervals from the center of the cornea (Figure 1), at 80 points in the 4 directions, using a speed-of-sound constant of 1550 m/second.[8,9]

Reproducibility of measurement. Measurement was done (as above) at 40 sites in 4 directions at 0.5 mm intervals from the corneal center in one eye of one volunteer by the same examiner on 5 different days; the same measurements were obtained in the same eye of one volunteer by four examiners on 1 day. The coefficient of variation (CV) was determined: $< 10\%$ was considered to indicate good reproducibility.[13]

Corneal thickness mapping. Corneal thicknesses measured in these eyes were processed with DeltaGraph Pro3.0J software (Delta Point, Monterey, CA, USA) on a personal computer (MacIntosh Quadra 950, Apple, Cupertino, CA, USA). A cornea was first projected as a coronal cross section from the front; the normal projection obtained was plotted on xy coordinates with the origin at the corneal center and the axes scaled upward and to the right. Next, the actual measurements were entered as two-dimensional coordinate data. Corneal thickness data were paired with coordinate data. Graphs were plotted with three-dimensional xyz coordinates. After plotting, the viewing angle was shifted to overlook the xy plane from directly above, using the three-dimensional display capability of the software. These steps produced a color map of the corneal thicknesses.

Results

Measurement of Corneal Thickness

Figure 2 shows corneal thicknesses in normal eyes ($n = 22$) measured at 0.5 mm intervals from the corneal center at 40 sites in 4 directions. The central thickness was 0.503 ± 0.027 mm (mean $\pm$ SD). The maximum CV of the measured values at each measurement point in the 22 eyes was 7%.

Reproducibility of Measurement

The CV was $\leq 6\%$ at all points for measurements by the same examiner in the same eye on 5 different days (Table 1), and $\leq 7\%$ for measurements on the same day by four different examiners (Table 2).

Corneal Thickness Mapping

Figure 3 shows corneal thickness maps of normal and morbid eyes.

Discussion

Accurate determination of the measuring points as well as precise measurement of the corneal thickness is essential for corneal thickness mapping. The

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Vol 41: 12–18, 1997

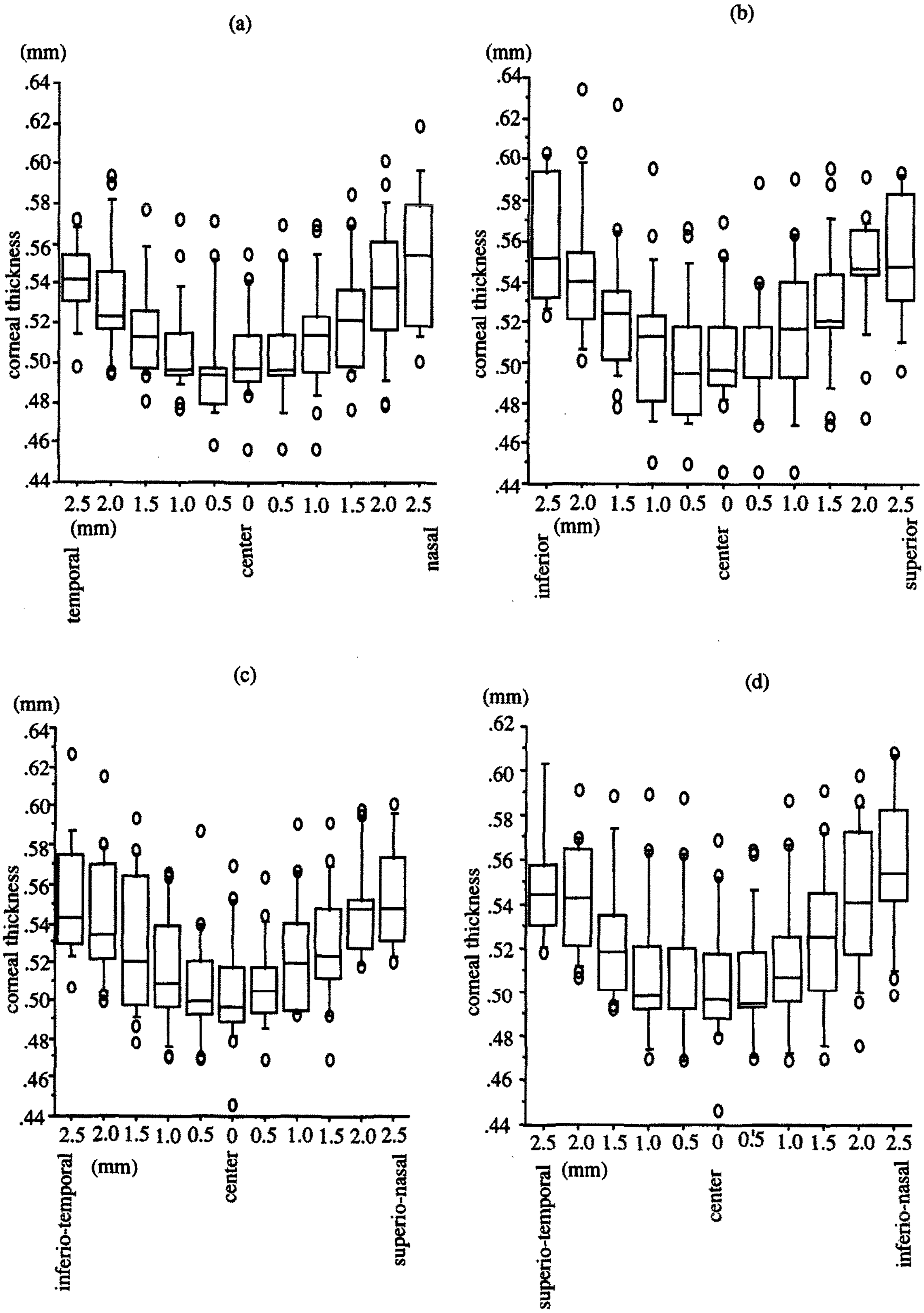

Figure 2. Corneal thickness in normal eyes: Box plots show corneal thickness in 22 normal eyes based on measurements at 40 sites at 0.5 mm intervals from the corneal center on 4 axes. (**A**) Temporal-nasal, (**B**) Inferior-superior, (**C**) Inferotemporal-superonasal, (**D**) Superotemporal-inferonasal.

Table 1. Reproducibility of Measurements: One Eye, Same Examiner on 5 Different Days

	Mean (mm)	SD	n	Min (mm)	Max (mm)	CV (%)
Temporal	0.54	0.01	4	0.53	0.56	2
	0.53	0.01	5	0.52	0.55	2
	0.50	0.01	5	0.49	0.53	3
	0.50	0.00	5	0.49	0.50	1
	0.49	0.01	5	0.47	0.49	2
Center	0.49	0.01	5	0.48	0.50	1
	0.49	0.01	5	0.47	0.49	2
	0.49	0.02	5	0.47	0.52	3
	0.50	0.01	5	0.49	0.52	2
	0.54	0.01	3	0.52	0.55	3
Nasal						
Superior	0.55		1	0.55	0.55	
	0.54	0.02	5	0.52	0.56	3
	0.50	0.01	5	0.49	0.52	3
	0.48	0.01	5	0.46	0.49	3
	0.48	0.01	5	0.47	0.49	2
Center	0.49	0.01	5	0.48	0.50	1
	0.49	0.01	5	0.47	0.50	3
	0.49	0.01	5	0.47	0.50	2
	0.50	0.02	5	0.49	0.53	3
	0.53	0.01	5	0.51	0.54	2
Inferior	0.55	0.03	4	0.52	0.58	5
Superonasal	0.54	0.01	3	0.52	0.54	2
	0.51	0.01	3	0.49	0.52	3
	0.50	0.02	5	0.47	0.52	4
	0.50	0.01	5	0.49	0.52	2
	0.49	0.02	5	0.47	0.52	4
Center	0.49	0.01	5	0.48	0.50	1
	0.49	0.02	5	0.47	0.51	4
	0.51	0.03	5	0.47	0.53	5
	0.52	0.03	5	0.47	0.55	6
	0.53	0.02	4	0.51	0.56	5
Inferotemporal	0.54	0.00	2	0.54	0.54	1
Superotemporal	0.56	0.02	2	0.54	0.58	4
	0.56	0.02	3	0.54	0.57	3
	0.52	0.02	5	0.49	0.55	5
	0.51	0.01	5	0.49	0.52	3
	0.49	0.02	5	0.46	0.52	4
Center	0.49	0.01	5	0.48	0.50	1
	0.49	0.01	5	0.48	0.48	1
	0.50	0.01	5	0.49	0.52	2
	0.51	0.02	5	0.49	0.54	4
	0.53	0.03	5	0.50	0.56	5
Inferonasal	0.55	0.01	4	0.55	0.56	1

Table gives mean and standard deviation of corneal thickness, number of examinations (n), maximum and minimum corneal thicknesses, and coefficient of variation (CV) of measurements (40 sites, 4 directions, 0.5 mm intervals from the corneal center).

Table 2. Reproducibility of Measurements: Different Examiners (n = 4)

	Mean (mm)	SD	n	Min (mm)	Max (mm)	CV (%)
Temporal	0.51		1	0.51	0.51	
	0.51	0.03	3	0.48	0.53	6
	0.50	0.03	4	0.46	0.52	6
	0.46	0.01	4	0.45	0.47	3
	0.45	0.01	4	0.45	0.47	2
Center	0.45	0.00	4	0.45	0.45	0
	0.45	0.00	4	0.45	0.45	0
	0.45	0.01	4	0.45	0.47	2
	0.47	0.01	4	0.45	0.47	3
	0.48	0.02	4	0.45	0.50	5
Nasal	0.52	0.02	3	0.50	0.55	5
Inferior	0.55		1	0.55	0.55	
	0.50	0.02	4	0.47	0.53	5
	0.48	0.02	4	0.45	0.50	5
	0.45	0.00	4	0.45	0.46	1
	0.45	0.00	4	0.45	0.45	0
Center	0.45	0.00	4	0.45	0.45	0
	0.45	0.00	4	0.45	0.45	0
	0.45	0.01	4	0.45	0.47	3
	0.47	0.02	4	0.45	0.50	4
	0.48	0.03	4	0.45	0.53	7
Superior	0.52	0.03	3	0.50	0.55	5
Inferotemporal	0.56		1	0.56	0.56	
	0.51	0.03	4	0.48	0.53	5
	0.49	0.02	4	0.47	0.52	5
	0.47	0.02	4	0.45	0.49	4
	0.47	0.02	4	0.45	0.49	5
Center	0.45	0.00	4	0.45	0.45	0
	0.46	0.02	4	0.45	0.49	5
	0.46	0.02	4	0.45	0.49	5
	0.49	0.02	4	0.47	0.52	4
	0.51	0.03	4	0.47	0.54	6
Superonasal	0.52	0.02	3	0.50	0.54	4
Superotemporal	0.57		1	0.57	0.57	
	0.54	0.02	3	0.53	0.57	5
	0.51	0.02	4	0.48	0.53	5
	0.49	0.02	4	0.47	0.52	4
	0.47	0.02	4	0.45	0.49	4
Center	0.45	0.00	4	0.45	0.45	0
	0.46	0.02	4	0.45	0.49	5
	0.47	0.03	4	0.45	0.50	6
	0.48	0.03	4	0.45	0.52	7
	0.50	0.03	4	0.47	0.53	6
Inferonasal	0.52	0.04	3	0.48	0.55	7

Measurements made in one eye by 4 examiners. Table gives mean and standard deviation of corneal thickness, number of examinations (n), maximum and minimum corneal thicknesses, and coefficient of variation (CV) of measurements (40 sites, 4 directions, 0.5 mm intervals from corneal center).

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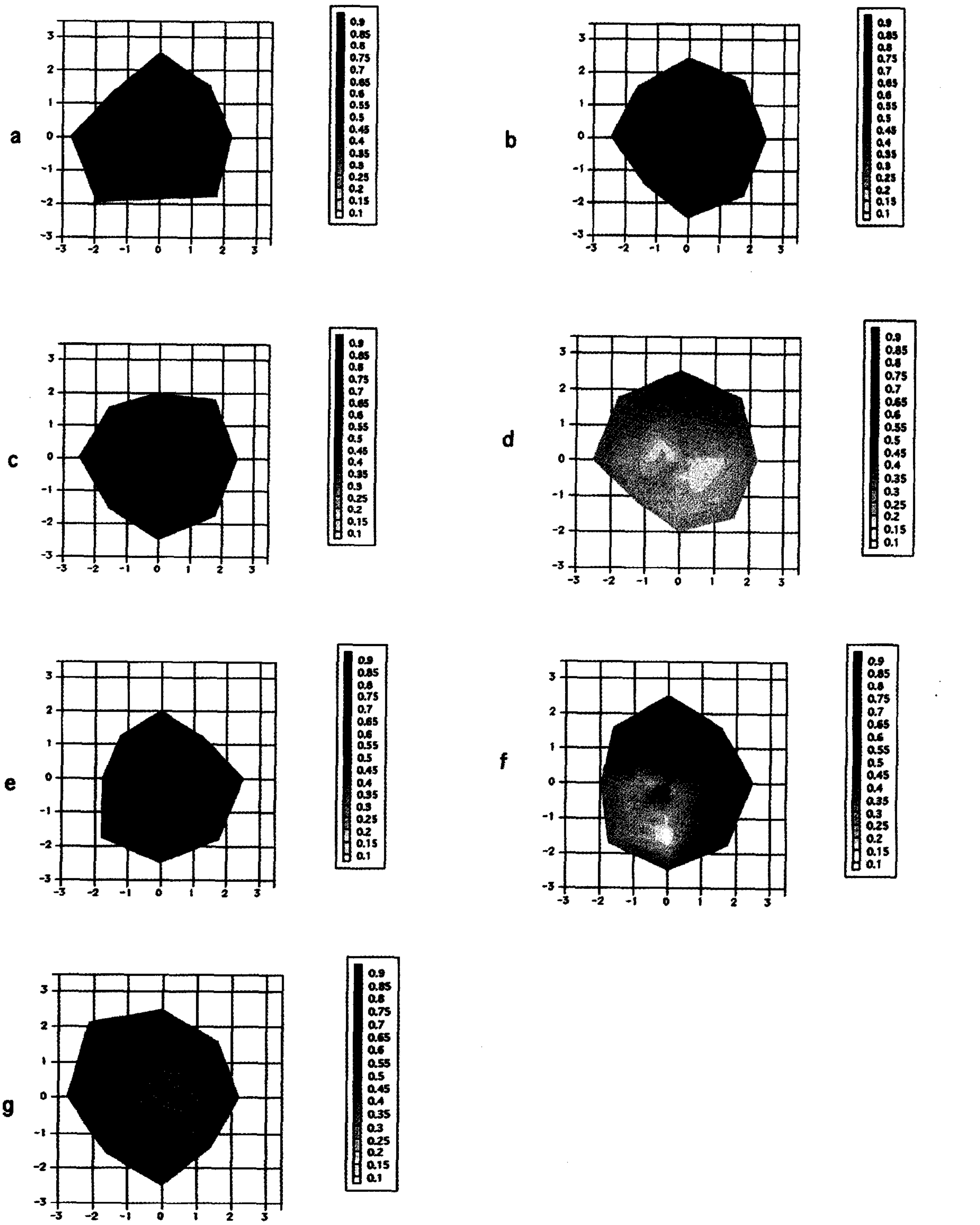

Figure 3. Corneal maps. (**A**) Normal left eye of 26-year-old female. Thinned area within 1 mm from center, thickness increased toward medial and superior directions of the periphery. Corneal thickness was 0.487 mm in the center and 0.544–0.568 mm in the periphery. (**B**) Right eye of a 46-year-old female with lattice corneal dystrophy. Cornea generally thicker than normal eye: 0.587–0.633 mm in the center, thickened to 0.677–0.702 mm in some lateral and medial areas. (**C**) Left eye of a 65-year-old male with granular corneal dystrophy. Area with reduced thickness of 0.450–0.543 mm < 1 mm from the center; corneal thickness gradually increased toward periphery. (**D**) Left eye of 18-year-old female with corneal herpes. Corneal thickness generally thinned in opacified areas of cornea; especially thin, 0.187–0.189 mm, 1 mm laterally from the center. Thickness of the area 5 mm diameter around the center was 0.187–0.496 mm, thinner inferiorly. (**E**) Right eye of a 78-

pachometer and specular microscope allow accurate measurement of the corneal thickness in the transparent central cornea, but do not provide accurate location data so that mapping with these techniques is unsatisfactory. There is also an ultrasonic pachometer of a contact type. With ultrasound biomicroscopy, however, measurement of corneal thickness can be done without touching the cornea, and locations can be determined even in a clouded cornea. The axial resolution of ultrasound imaging is determined by the ultrasound frequency and interval.[6,7,10] Theoretically, UBM with a frequency of 50 MHz has an axial resolution 2.5–5 times higher than currently used scanners, which have a 10 MHz frequency with combined A-B scans, or ultrasound pachometers with a frequency of 20 MHz; UBM makes more accurate corneal thickness mapping possible.[8] Measurement accuracy in ultrasound biomicroscopy is limited by the lateral and axial resolution of the system, the stability of the mechanical motion, and the pixel size of the image. Axial resolution refers to the instrument's capability to distinguish between two surfaces as they are brought closer together.

Measurement precision can be significantly better than the axial resolution might indicate when the two planar interfaces are well resolved and parallel (anterior and posterior corneal surfaces).[7] Although a change in corneal thickness during a single day was reported, no clinical differences were found with the various measurement times.[11] No significant difference in corneal thickness was found between the left and right eyes, regardless of sex.[1] Ultrasound passes through air very poorly; the fluid used should have low sound attenuation. We use ethylcellulose for most examinations because of its minimal sound attenuation. For all practical purposes, changes in refractive index caused by the fluid used result in only a negligible error in thickness measurement in vivo.[7]

According to the mean corneal thickness in 22 normal eyes, the cornea was thinnest in the center and thicker toward the margins, despite individual differences, as reported by Kato et al.[12] The maximum CV was 7%, indicating a certain degree of regularity. Tello et al[13] reported that the CV of the central corneal thickness was 3% and that reproducibility is satisfactory when the CV is $< 10\%$. Our results give a CV for the central corneal thickness of 1%: it was $\leq 6\%$ on measurements (central and peripheral) by the same examiner, and $\leq 7\%$ on measurements by different examiners. From these observations, our measurement of corneal thickness with UBM is highly reproducible and reliable.

We have been able to create a corneal thickness map using UBM data, which indicates that there are individual variations in the corneal thickness. One component of this method is the time difference between reflected ultrasound from the front and back of the cornea. This time difference, multiplied by the ultrasound velocity as it passes through the cornea, gives the corneal thickness measurement. A question may arise because different velocities have been reported, ranging from 1500 to 1640 m/seconds.[11] However, this applies to all ultrasonic pachometers: the transducer must be placed vertically over the cornea. A geometric error of 5° from the vertical axis would be 0.38%; 10° would be 1.54% of the corneal thickness. Variations in corneal thickness from small deviations of fixation were minimized in our study by requesting the subject to focus on a point on the ceiling during scanning. Errors from slightly eccentric fixation produce only negligible errors in corneal thickness measurements.[10]

Corneal thickness mapping can now contribute to the evaluation of the cornea following refraction surgery or in pathologic conditions to evaluate postoperative healing.

The author wishes to thank Prof Y. Uji for his interest and suggestions throughout this research. The author is also grateful to Drs K. Emi and H. Ishikawa for their valuable guidance and collaboration.

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year-old man with bullous keratopathy. Corneal thickness was generally increased to ≥ 0.9 mm especially in lower area. **(F)** Right eye of 35-year-old man with keratoconus. Thinned area extended from center to medioinferior direction; thickness near apex of keratoconus (1.5 mm medioinferiorly from center) was reduced to 0.143–0.252 mm. **(G)** Right eye of a 47-year-old woman with a history of posterior keratotomy for keratoconus. Cornea was flattened; almost even thickness: 0.330–0.435 mm to 1 mm from center; 0.445–0.549 mm in peripheries.

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