ORIGINAL RESEARCH

Study of Inter observer and Intra observer reproducibility of central corneal thickness measurements by using ultrasonic pachymetry

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ABSTRACT

Background: Measurement of central corneal thickness (CCT) is highly useful for both diagnostic and therapeutic assessment purposes. CCT is helpful in diagnosis and progression of certain corneal disease such as Fuch's corneal endothelial dystrophy.Present study was aimed to study Inter observer and intraobserver reproducibility of central corneal thickness measurements by using commercial available ultrasonic Pachymeter. **Material and Methods:** Present study was single-center, prospective, observational study, conducted in individuals of age 40 to 80 years, attending glaucoma clinic, irrespective of whether they have glaucoma or not. PACSCAN 300AP of Sonomed, an ultrasonic pachymeter is used for this study. All the subjects underwent pachymetry as described above by three observers. **Results:** In present study, among 40 subjects, 17 were female and 23 were male. All of them underwent pachymetry in both of their eyes, thus a total of 80 eyes were included in the study. The mean CCT of observer A, observer B & observer C was 532.8µm, 528.3µm & 530.1µm respectively. There is no significant difference between the three mean CCT measurements (p=0.7). By Bland–Altman plot, the limits of agreement are narrow with respect to the mean CCT, thus indicating excellent agreement. The mean measurement difference between observers was 2.91µm and the mean expected Inter observer measurement was within ±1.00% and the largest observed value was < ±1.1%. The ICC for reproducibility study was 0.979 (p<0.0001)suggesting that there is significant correlation between mean of the observer A, Observer B and Observer C. For the observer A, the ICC was 0.967(p-value<0.0001) suggesting there is a significant correlation between 3 CCT measurements. **Conclusion:** A variation of ≥15 mm between two repeated measurements occurred in 20.14% test-retest Inter observer evaluations, and in 30.93% test-retest Intra observer evaluations. This indicates that, despite the high reproducibility of the procedure.

Key words: Central corneal thickness (CCT), corneal disease corneal changes, ultrasound pachymetry

INTRODUCTION

Central corneal thickness (CCT) is an important indicator of health status of the cornea especially of corneal barrier and endothelial pump function. Measurement of central corneal thickness (CCT) is highly useful for both diagnostic and therapeutic assessment purposes. CCT is helpful in diagnosis and progression of certain corneal disease such as Fuch's corneal endothelial dystrophy[1].

Accurate measurement of corneal thickness is of paramount importance for preoperative assessment and planning of all keratorefractive surgical procedures. In addition CCT measurement is an important diagnostic tool to monitor corneal changes after extended contact lens wear.[1] Apart from corneal diseases, CCT plays an important role in estimating the reliability of intraocular pressure measurements[2, 3].

Different devices available for measuring the corneal thickness are based on a variety of techniques and each has its own advantages and disadvantages. Despite the new pachymetric techniques available, ultrasound pachymetry is most commonly accepted because of accuracy and easy to handle[4]. Present study was aimed to study Inter observer and Intra observer reproducibility of central corneal thickness measurements by using commercial available ultrasonic Pachymeter.

MATERIAL AND METHODS

Present study was single-centre, prospective, comparative, parallel-group, observational study, conducted in Postgraduate institute of ophthalmology, at Aravind Eye Hospital, Madurai, India. Study duration was of 2 years (January 2008 to December 2009). Study approval was obtained from institutional ethical committee.

Inclusion criteria

- All individuals of age 40 to 80 years, attending glaucoma clinic, irrespective of whether they have glaucoma or not, willing to participate in present study

EXCLUSION CRITERIA

- Individuals with previous corneal surgery.
- Individuals with previous or current corneal disease including pterygium.
- Any active ocular infection or inflammation.
- Contact lens wearers.
- Patients with astigmatism greater than 1.5 D.
- Pregnancy.

Study was explained to patients in local language & written consent was taken for participation & study. All patients were enquired about relevant clinical history and undergone slit lamp examination along with refraction. The steps of the procedure were explained to patient in his or her own language. PACSCAN 300AP of Sonomed, an ultrasonic pachymeter is used for this study. It is a portable device which consists of a pacscan unit which is attached to an ultrasonic probe.

Lignocaine 4% eye drop was used in all cases as the topical anaesthetic agent. Subjects were seated and asked to look forward and fixate on a distant target. The measurement technique involved placing the tip of the hand held probe perpendicular to the center of the cornea, using the center of the undilated pupil as the landmark. The probe should gently touch the surface of the cornea. An automatic reading will be taken by the pachymeter after pressing the 'START' button. Another four readings are taken with the standard deviations. Eliminating the first and fifth reading the mean of second, third and fourth readings were calculated as mean CCT of an individual.

In order to reduce the possibility of ocular surface drying, one drop of artificial tear (Moisol eye drop) was instilled 30 seconds before each measurement. Each measurement was recorded by an assistant. The observers were masked for all CCT measurements. The probe was sterilized with alcohol after each subject.

All the subjects underwent pachymetry as described above by three observers (ophthalmic assistant, resident and glaucoma fellow) who had experience in the use of the instrument. The order in which the observers took the measurements was randomized. The time interval between each observer was less than five minutes to reduce the effect of diurnal variation on CCT. Inter observer reproducibility was based on the analysis of the three independent series of measurements made by the three examiners (nine readings).

Intra observer reproducibility was calculated for each of the three observers on the basis of three consecutive measurements done by them for all the above 40 subjects in both eyes. The time interval between each measurement was less than five minutes.

Data was collected and compiled using Microsoft Excel, analysed using SPSS 23.0 version. Difference of proportions between qualitative variables were tested using chi- square test or Fisher exact test as applicable. P value less than 0.5 was considered as statistically significant. The Intra observer repeatability and Inter observer reproducibility were calculated by means of intraclass correlation coefficient (ICC).

RESULTS

In present study, among 40 subjects, 17 were female and 23 were male. All of them underwent pachymetry in both of their eyes, thus a total of 80 eyes were included in the study. The mean age of the subjects was 56.8 ± 7.88 years, with a range of 40 to 72 years.

Table 1: General characteristics

	No. of patients	Percentage
Age groups (in years)		
40-50	10	25
51-60	17	42
61-70	12	30
>70	1	2.5
Mean age (mean ± SD)	56.8 ± 7.88	
Gender		
Male	23	57
Female	17	43

The mean CCT of observer A, observer B & observer C was 532.8µm, 528.3µm & 530.1µm respectively. There is no significant difference between the three mean CCT measurements (p=0.7). To assess agreement between the observers, Bland–Altman plot was constructed. It can be seen that the limits of agreement are narrow with respect to the mean CCT, thus indicating excellent agreement.

Table 2: Inter observer reproducibility

	Mean	Std. Deviation	Minimum	Maximum
CCT A1	533.24	34.317	456	601
CCT A2	533.71	35.433	453	601
CCT A3	531.22	35.431	453	614
Mean A	532.78	34.742	454	605
CCT B1	527.92	33.509	449	592
CCT B2	528.79	35.201	449	601
CCT B3	528.38	32.961	460	591
Mean B	528.31	33.179	462	592
CCT C1	529.65	33.515	453	601
CCT C2	529.31	35.554	402	601
CCT C3	529.98	32.764	453	601
Mean C	530.09	32.563	458	601

The mean measurement difference between observers was 2.91µm and the mean expected Inter observer measurement was within ±1.00% and the largest observed value was < ±1.1%.

The ICC for reproducibility study was 0.979 (p<0.0001)suggesting that there is significant correlation between mean of the observer A, Observer B and Observer C.

Table 3: Differences between the test-retest and their confidence intervals

Test-retest	ICC	Mean	Difference	SD	95% CI	95% CI (%)
Interobserver						
obsA1-obsB1	0.934	530.58	5.31	5.36	525.29-535.88	1.00
obsA1-obsB2	0.936	531.01	4.45	5.5	525.6-536.43	1.02
obsA1-obsB3	0.922	530.81	4.86	5.32	525.56-536.06	0.99
obsA1-obsC1	0.9	531.44	3.6	5.36	526.16-536.73	0.99
obsA1-obsC2	0.823	531.28	3.93	5.52	525.83-536.72	1.03
obsA1-obsC3	0.913	531.61	3.26	5.3	526.38-536.83	0.98
obsA2-obsB1	0.926	530.82	5.79	5.45	525.43-536.21	1.02
obsA2-obsB2	0.933	531.25	4.93	5.58	525.74-536.76	1.04
obsA2-obsB3	0.921	531.04	5.34	5.41	525.7-536.39	1.01
obsA2-obsC1	0.902	531.68	4.06	5.45	526.3-537.06	1.01
obsA2-obsC2	0.831	531.51	4.4	5.61	525.98-537.05	1.04
obsA2-obsC3	0.893	531.84	3.74	5.4	526.52-537.16	1.00
obsA3-obsB1	0.945	529.58	3.3	5.45	524.2-534.92	1.02
obsA3-obsB2	0.943	530	2.44	5.58	524.51-535.51	1.04
obsA3-obsB3	0.931	529.8	2.85	5.41	524.47-535.13	1.01
obsA3-obsC1	0.907	530.44	1.58	5.45	525.07-535.81	1.01
obsA3-obsC2	0.846	530.27	1.91	5.61	524.72-535.8	1.05
obsA3-obsC3	0.909	530.6	1.25	5.4	525.29-535.91	0.91
obsB1-obsC1	0.924	528.79	1.73	5.3	523.57-534	0.99
obsB1-obsC2	0.873	528.62	1.39	5.46	523.24-534	1.02
obsB1-obsC3	0.922	528.95	2.05	5.24	523.79-534.11	0.98
obsB2-obsC1	0.917	529.22	0.86	5.43	523.87-534.57	1.01
obsB2-obsC2	0.866	529.05	0.53	5.59	523.54-534.56	1.04
obsB2-obsC3	0.91	529.38	1.19	5.38	524.09-534.67	1.00
obsB3-obsC1	0.951	529.01	1.28	5.26	523.84-534.19	0.98
obsB3-obsC2	0.89	528.84	0.94	5.42	523.51-534.18	1.01
obsB3-obsC3	0.934	529.18	1.6	5.2	524.06-534.29	0.97
Mean	0.907	530.24	2.91	5.42		1.00

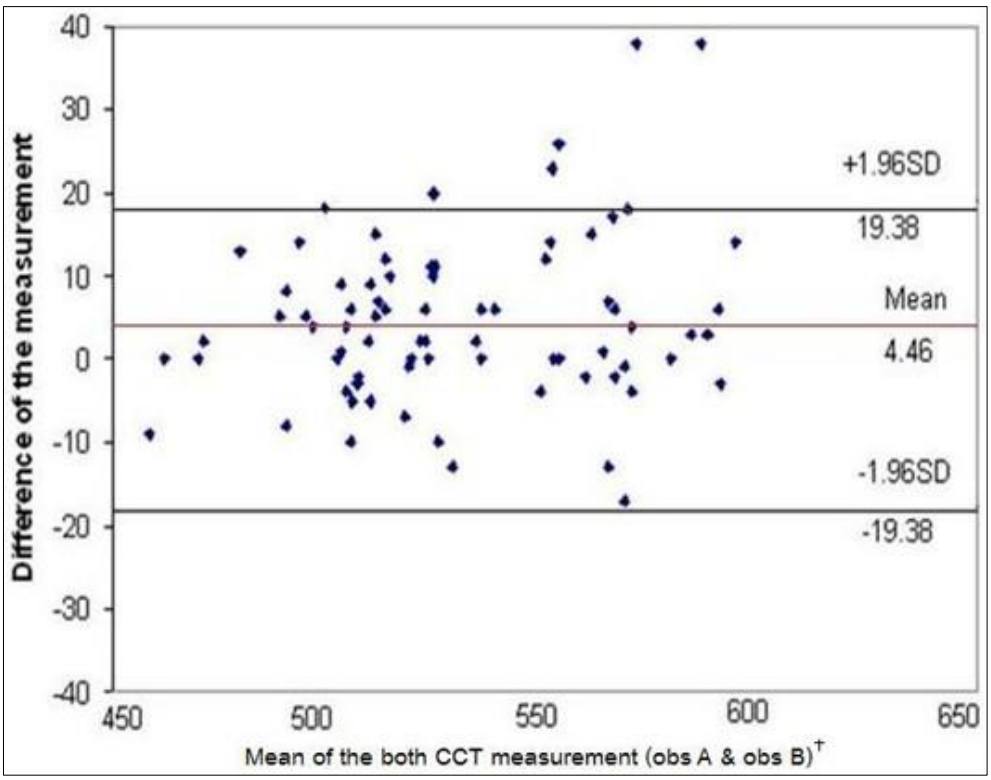

Fig 1: A Bland-Altman plots of data from the Inter observer reproducibility study. Mean of both CCT measurements was plotted against the difference in the mean CCT measurement between observer A and B. The red line represent mean difference and the two black lines represent upper and lower borders of the 95% limits of agreement (mean difference±1.96 standard deviation of the mean difference)

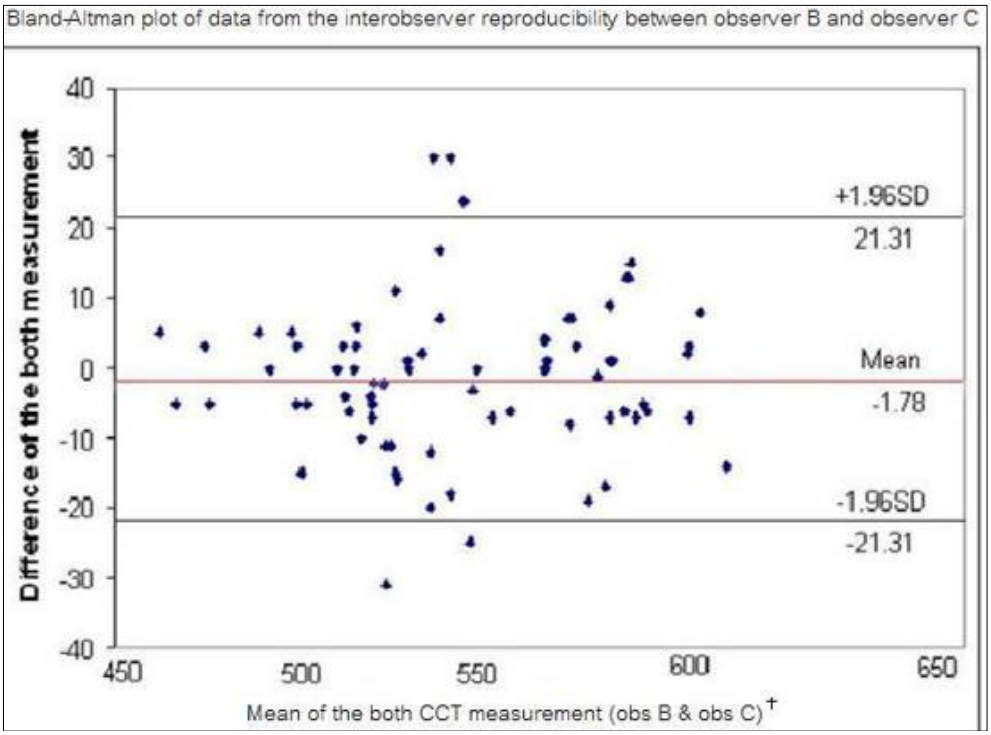

Fig 2: A Bland- Altman plots of data from the Inter observer reproducibility study. Mean of both CCT measurements was plotted against the difference in mean CCT measurement between observer B and C. The red line represent mean difference; the two black lines represent upper and lower borders of the 95% limits of agreement (mean difference±1.96 standard deviation of the mean difference)

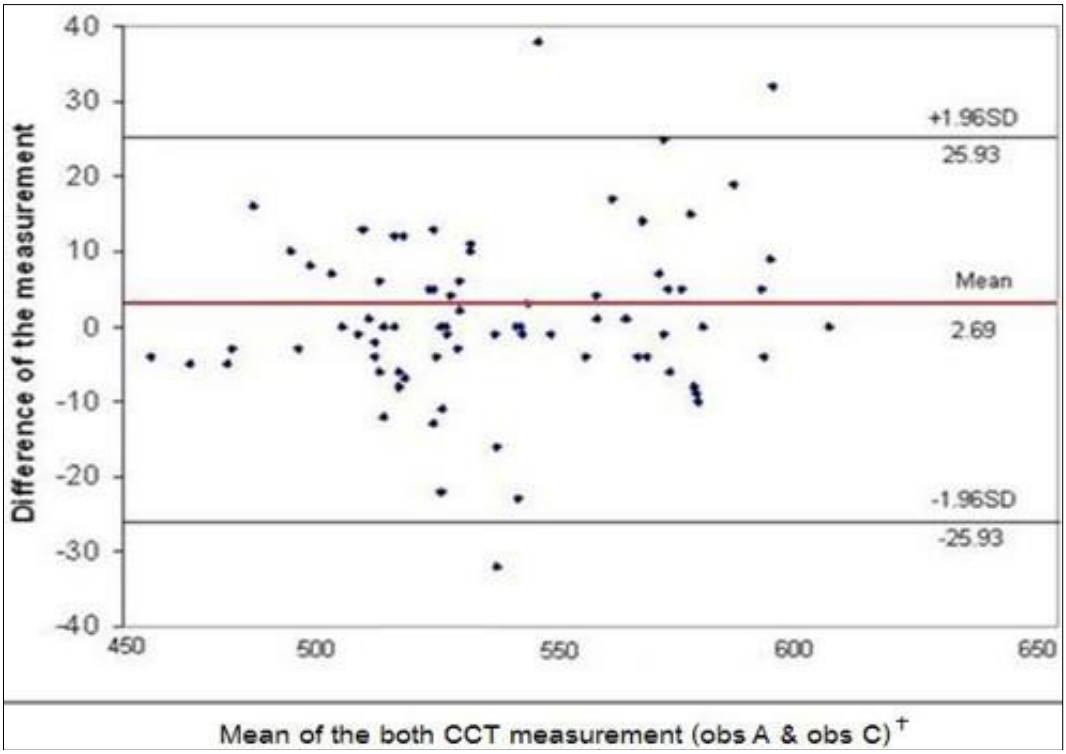

Fig 3: A Bland- Altman plots of data from the Inter observer reproducibility study results. Mean of the both CCT measurement was plotted against the difference in mean CCT measurement between observer A and C. The red line represent mean difference; the two black lines represent upper and lower borders of the 95% limits of agreement (mean difference±1.96 standard deviation of the mean difference)

For the observer A, the ICC was 0.967(p-value<0.0001) suggesting there is a significant correlation between 3 CCT measurements. For the observer B, the ICC was 0.97(p-value < 0.0001) suggesting there is a significant correlation between 3 CCT measurements. For the observer C, the ICC was 0.93 (p-value<0.0001) suggesting there is a significant correlation between 3 CCT measurements. The mean ICC for Intra observer reproducibility was 0.956 (SD 0.022) and 95% CI was within 0.915 - 0.974. The mean expected Intra observer measurement was within ±1.01% and the largest observed value was < ±1.1%. The above all results indicated statistically excellent correlation.

Table 4: Intra observer repeatability

Test-retest	ICC	Mean	Difference	SD	95% CI	95% CI (%)
Intra observer						
obsA1-obsA2	0.963	533.48	0.48	5.51	528.05-538.9	1.02
obsA1-obsA3	0.964	532.23	2.01	5.51	526.8-537.66	1.02
obsA2-obsA3	0.974	532.47	2.49	5.6	526.95-537.95	1.04
obsB1-obsB2	0.972	528.36	0.86	5.43	523.0-533.7	1.01
obsB1-obsB3	0.965	528.15	0.45	5.26	522.98-533.32	0.98
obsB2-obsB3	0.972	528.58	0.41	5.39	523.27-533.89	1.00
obsC1-obsC2	0.924	529.48	0.34	5.46	524.10-534.86	1.02
obsC1-obsC3	0.957	529.81	0.33	5.24	524.65-534.97	0.97
obsC2-obsC3	0.915	529.64	0.66	5.41	524.32-534.97	1.00
Mean	0.956	530.24	0.89	5.42		1.01

The average CCT in males and females was 537.4µ & 526.5µ for observer A. Similarly for observer B was 532.6µ & 522.6µ respectively. For observer C, the average CCT in males and females was 532.2µ &527.2 µ respectively. There is no gender-related difference between CCT measurements in all 3 Observers.

Table 5: Gender wise observer variability

Mean CCT	Sex	No of eyes	Mean	Std. Deviation	Std. Error Mean	p-value
Obs A	Male	46	537.39	32.604	4.807	0.168
	Female	34	526.53	37.015	6.348	

Obs B	Male	46	532.57	32.482	4.789	0.184
	Female	34	522.56	33.725	5.784	
Obs C	Male	46	532.24	33.127	4.884	0.495
	Female	34	527.18	32.043	5.495	

There is no significant difference between age category in observer A (p-value=0.23). There is no significant difference between age category in observer B (p-value=0.24). There is no significant difference between age category in observer C (p-value=0.37).

Table 6: Age wise observer variability

Age	Mean CCT of Obs A(Mean 1)	Mean CCT of Obs B(Mean 2)	Mean CCT of Obs C(Mean 3)
40-50	544.1	538.3	538.5
51-60	529.1	523.2	527.9
61-70	526.5	524.9	524.3
>70	557.5	556	552.5

DISCUSSION

Many studies have reported the precision analysis of CCT measurement. Some studies analyzed the agreement between contact and noncontact techniques while others compared ultrasound pachymetry with coherence interferometry and optical coherence tomography[5, 6]. Few recent studies have reported that measurement of CCT by means of ultrasonic pachymetry is highly repeatable and reproducible, although most of them used small sample size[7, 8].

There is considerable amount of published data suggesting a relationship between CCT and the risk of glaucoma[4].The mean ICC for Intra observer reproducibility was 0.956 (SD 0.022) and 95%CI from 0.915 - 0.974. The mean ICC for Inter observer reproducibility was 0.907 (SD 0.034) and 95% CI from 0.823 - 0.951.

The mean expected Intra observer measurement was within ±1.01% and the largest observed value was <±1.1%.The mean expected Inter observer measurement was within ±1.00% and the largest observed value was <±1.1%. The extent of variability between each test-retest did not depend on the absolute CCT value in any comparison, both in the Intra observer and Inter observer evaluations.

Bland- Altman plots of data from the Inter observer reproducibility study also showed narrow limits of agreement. Thus the analysis of Intra observer repeatability and Inter observer reproducibility shows almost perfect correlation. All the above results indicate that both the Intra observer and Inter observer reproducibility of CCT measurements is extremely high. Our results were consistent with the previous published studies:

S.Migilor*et al.*,[9] reported that the mean CCT of 51 subjects were 568 ±12 µm. The ICC was 0.966(SD 0.009) for Intra observer reproducibility study and 0.935(0.016) for Inter observer reproducibility study. The ICCs of the intra- and Inter observer analyses were significantly different (p<0.0001). Although similar, the mean measurements made by the three observers also were statistically different (p=0.002). They concluded that Intra observer and Inter observer reproducibility of CCT measurements is extremely high. Though we also used a probe of 1 mm and there was no any fixation light but we did not have any statistical significant difference between the three mean CCT measurements.

WeerawatKiddee*et al.*,[10] reported that the mean CCT of 35 subjects (70 eyes) was 537.61±26.66µm. The analysis of Intra observer repeatability and Inter observer reproducibility showed almost perfect correlation (ICC being between 0.935 and 0.985). The strength of linear relationship was more than 0.8 thus suggesting a "very strong correlation". The results show that the CCT measurements made by different operator may be slightly different but still in narrow limit of agreement. They concluded that the measurement of CCT using the ultrasonic pachymeter is highly repeatable and reproducible.

Similarly, Gunvant P *et al.*,[11] studied the repeatability and reproducibility of CCT by BVI ultrasonic pachymeter. The mean CCT of 72 subjects was 538µm (95% CI 528- 545). The ICC of 42 eyes was 0.996 for Inter observer repeatability and the ICC of 40 eyes was 0.99 for Intra observer reproducibility. The Intra observer and Inter observer level of agreement was excellent with a mean difference between measurements were only 0.7mm & 0.9mm respectively. The BVI Pocket Pachymeter showed excellent Inter observer and Intra observer reliability.

The sources of variability may be the cooperation of subject and the corneal touch technique (such as differing forces of probe placement by different observers and slightly off-center probe placement). The previously demonstrated diurnal variation of CCT would not have been a factor in our study because the time interval between measurements was short.

CONCLUSION

A variation of ≥15 mm between two repeated measurements occurred in 20.14% test-retest Intra observer evaluations, and in 30.93% test-retest Inter observer evaluations. This indicates that, despite the high reproducibility of the procedure, care should be taken in the interpretation of IOP measurement corrected on the basis of CCT measurement.

CONFLICT OF INTEREST: None to declare.

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