Normative Data of Macular Thickness Using Spectral Domain Optical Coherence Tomography for Healthy Jordanian Children

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Purpose: To report normative values of macular thickness and volume by spectral-domain optical coherence tomography (SD-OCT) in the eyes of healthy Jordanian children aged 6–16 years and assess the correlation of macular parameters with age, sex, and refractive error.

Patients and Methods: This observational study included 144 eyes of 144 healthy children. All children underwent comprehensive ocular examination and cycloplegic refraction. Average macular thickness, macular volume, central subfield thickness (CST), and macular thickness for all the Early Treatment Diabetic Retinopathy Study (ETDRS) quadrants were obtained using Primus SD-OCT (Carl Zeiss Meditec).

Results: The study group consisted of 68 boys and 76 girls with a mean age (SD) of 10.8 (3.0) years. The mean (SD) spherical equivalent refraction (SER) was 0.56 (1.73) diopters (range: −4.75 to 4.75). The mean of macular average thickness was 277.2±12.5 μm, and the mean of the central subfield thickness was 246.7±16.8 μm. In multivariate analysis, all macular parameters except the central subfield thickness (CST) correlated positively with the SER. Boys had significantly higher CST than girls (p=0.008). None of the macular parameters were correlated with age.

Conclusion: Normative data of macular thickness for healthy Jordanian children were established for sex and age groups using SD-OCT.

Keywords: central subfield thickness, macular thickness, normative data, pediatric OCT, Primus OCT

Introduction

Optical coherence tomography (OCT) is a well-established method for acquiring high-resolution images of the retina and optic disc. Its main advantages include being noninvasive, objective, reliable, with good repeatability and reproducibility1 in both adult and pediatric populations. Besides providing a morphological assessment of the retina and optic disc, it also provides accurate quantitative measurements that help diagnose and monitor the progression or response to treatment of many retinal pathologies.

Despite the expected difficulties when performing OCT in children, where it requires a certain degree of cooperation and attention, OCT has proven to be well tolerated in children and has many clinical applications in pediatric retinal and optic disc pathologies.2 Different OCT machines come preloaded with normative data on retinal parameters for adults (18 years and older) derived from certain ethnic groups, but not for children, and this may limit the value of OCT in the pediatric setup since the diagnosis of early retinal or optic disc pathologies requires knowledge of normal OCT values of the studied tissue. Many published papers reported such normative data on macular thickness and volume in normal children among different ethnic groups using spectral-domain OCT (SD-OCT), and the reported data varied with race and other factors, however, only two reports come from the Middle East.3,4 To the best of our knowledge, normative macular thickness OCT data for Jordanian children have not been published previously.
The purpose of this study was to report normative data on macular thickness and volume measured by SD-OCT in normal eyes of healthy children in Jordan and assess its correlation with age, sex, and refractive error.

**Materials and Methods**

**Design and Study Population**
An observational study was performed on 144 consecutive healthy Middle Eastern children aged between 6 and 16 years who presented to a comprehensive ophthalmic outpatient clinic in Irbid, Jordan. The study adhered to the tenets of the Helsinki declaration and was approved by the Jordan University of Science and Technology Institutional Review Board. Informed written consent was signed by parents (guardian) of the participating children.

The participating children attended the eye clinic for routine refraction, or for vision screening on the request of parents or school, and were healthy, born term (≥37 weeks gestational age), with no history of systemic metabolic or CNS diseases, no history of ocular abnormalities such as retinal or optic nerve pathology, corneal diseases, strabismus, amblyopia, glaucoma, no history of significant ocular trauma and no history of intraocular surgery. Children were also included if they had monocular best corrected visual acuity of 1.0 in both eyes (Snellen’s chart or the Tumbling E chart), normal anterior and posterior segment examination, and no abnormality of extraocular motility and ocular alignment examination.

We excluded children with high refractive errors of more than ± 5 diopters of spherical equivalent refraction (SER), anisometropia >1.5 diopters SER, children with abnormally looking foveal reflex, optic discs with a cup/disc ratio >0.5 (or >0.2 asymmetry between the two eyes), optic disc anomalies such as a tilted disc, and uncooperative children for OCT imaging.

Demographic data was recorded including age, sex, general medical history, and family history of inherited ophthalmic diseases. The children were separated into three groups according to age; group 1: <10, group 2: 10–12, and group 3: >12 years.

**Ocular Examination**
All participating children underwent a standard ophthalmic examination. Best corrected visual acuity was recorded monocularly using the Snellen’s chart or the Tumbling E chart, followed by assessment of ocular alignment, extraocular motility testing, and anterior segment examination with a slit lamp. All children underwent cycloplegic refraction using cyclopentolate 1% eye drops instilled in each eye 10 minutes apart. Cycloplegic refraction was measured 50 minutes after the last drop using an autokeratorefractometer (ARK-1s, Nidek, Aichi, Japan), which provides the median of at least 3 measurements. Astigmatism was recorded as the negative cylinder and spherical equivalent refraction was calculated according to the equation: SER = sphere power +(1/2 cylinder power). Dilated fundus examination was then performed using slit-lamp biomicroscopy and indirect ophthalmoscopy.

**OCT Measurement**
The Primus SD-OCT machine (Carl Zeiss Meditec AG, Germany, model 200, software version 3.0) was used to acquire macular OCT images through the dilated pupil. It acquires retinal images using a super luminescent diode with a wavelength of 840 nm at a scanning speed of 12,000 A-scans per second and has an axial tissue resolution of 5 μm and a transverse resolution of ≤20 μm. The device has been shown to have good repeatability and reproducibility for both normal and diseased eyes. Additionally, there was a substantial equivalence between the PRIMUS 200 and Cirrus HDOCT Model 4000, and a substantial level of agreement in normative limits between normative databases of Primus 200 and Cirrus for the measurement parameters obtained from a given subject.

The macular thickness analysis scan protocol generates a cube of data through a 6 mm square grid centered on the fovea by acquiring a series of 32 horizontal scan lines each composed of 512 A-scans. The machine displays the thickness measurements over a circular map which is a modified ETDRS (Early Treatment Diabetic Retinopathy Study) Grid and calculates the total macular volume and overall macular average thickness for the ILM-RPE tissue layer over the entire 6 mm square scanned area. The modified ETDRS grid map shows overall average thickness in nine sectors. This circular map is automatically centered on the fovea and is composed of three concentric circles: the central circle with a diameter of 1 mm corresponding to the foveal central 1mm circle, and its thickness is referred to
as Central Subfield Thickness (CST), the inner circle, 3 mm in diameter, and the outer circle 6 mm in diameter. Both inner and outer circles are divided into superior, nasal, inferior and temporal quadrants. The macular thickness analysis map obtained by the Primus OCT of the measured and calculated macular parameters is shown in Figure 1.

All OCT scans were performed by a single experienced operator utilizing the same OCT machine and during the same day of conducting ocular examination and cycloplegic refraction. The right eye was scanned first followed by the left eye. Internal fixation light was used, and the procedure carried out in a dim room. Three to four images were taken for each eye and then reviewed individually by the operator. Images with poor signal strength (less than 7/10), poorly centered, those with motion artifacts, and images with dark areas were excluded with the purpose of having at least 2 images with acceptable quality.

The two authors reviewed all images and by consensus, selected the image with the highest signal strength, best centration, and no missing data.

Statistical Analysis
The data from the left eye were used for analysis and were analyzed using the Statistical Package for the Social Sciences (SPSS) version 26 (IBM corporation, Armonk, NY, USA). The normality of distributions for the measured macular parameters were tested using the Shapiro–Wilk test. Mean (± standard deviation) as well as 5th and 95th percentiles were used to describe the macular parameters. Percentages were used to describe categorical variables. Pearson correlation was used to test the correlation between the measured macular parameters and other variables. The generalized linear model (GLM) multivariate procedure was used for testing the effect of different variables on macular parameters. The GLM Multivariate procedure provided regression analysis and analysis of variance for multiple macular parameters by sex, age, and SER. A p-value of less than 0.05 was considered statistically significant.

Results
The data on the left eyes of 144 children (68 boys and 76 girls) were analyzed. Their age ranged from 6 years to 16 years with a mean (SD) age of 10.8 (3.0) years. A total of 49 (34%) children aged <10 years, 49 (34%) aged between 10 and 12 years, and
46 (31.9%) aged >12 years. The mean (SD) spherical equivalent refraction was 0.56 (1.73) diopters (Range: −4.75 to 4.75). Table 1 shows sex and spherical equivalent refraction according to age groups. The mean of macular average thickness was 277.2±12.5 μm, and the mean of the central subfield thickness was 246.7±16.8 μm. The macular thickness measurements in the 9 ETDRS grid sectors, the average macular thickness, and the total macular volume according to age groups and sex are shown in Table 2.

All the macular measurements, average macular thickness, and the total macular volume were weakly and positively correlated with the SER (p<0.05) except the central subfield thickness (p =0.79).

Using the GLM Multivariate Analysis (Table 3), age was not significantly associated with all studied macular parameters. There was no significant sex difference in all parameters, except for central subfield thickness. The adjusted mean of central subfield thickness was significantly higher in boys (250.68 μm (95% CI: 246.68, 254.68)) compared to girls (243.06 μm (95% CI: 239.29, 246.84)). As the SER increased, all macular parameters, except central subfield thickness, significantly increased. There was no significant interaction between age, sex, and SER for all macular parameters. The overall sex, age, and SER adjusted means of all macular parameters are shown in Table 4.

### Table 1 Sex and Spherical Equivalent Refraction According to Age Groups

| Age Group (Years) | Gender (Girls, %) | Spherical Equivalent Refraction |
|-------------------|-------------------|--------------------------------|
|                   |                   | Mean (SD)                      | Range  |
| < 10              | 20 (40.8)         | 1.04 (1.57)                    | −4.63  | 4.75  |
| 10–12             | 24 (49)           | 0.46 (1.70)                    | −3.88  | 3.88  |
| > 12              | 32 (69.6)         | 0.17 (1.83)                    | −4.75  | 4.75  |

### Table 2 Normative Values of Macular Parameters According to Sex and Age Groups

| Macular Parameters | Age Group (Years) | Total |
|-------------------|-------------------|-------|
|                   | <10               | 10–12 | >12  |       |
|                   | Mean  | Percentile | Mean  | Percentile | Mean  | Percentile | Mean  | Percentile |
|                   | 5th   | 95th       | 5th   | 95th       | 5th   | 95th       | 5th   | 95th       |
| Macular Volume (mm³) |      |            |      |            |      |            |      |            |
| Male              | 10.0  | 9.2        | 10.0  | 9.4        | 9.9   | 9.3        | 10.5  | 9.3        |
| Female            | 10.0  | 9.4        | 10.0  | 9.2        | 9.9   | 9.1        | 10.5  | 9.2        |
| Total             | 10.0  | 9.3        | 10.0  | 9.2        | 9.9   | 9.3        | 10.5  | 9.2        |
| CST (μm)          |      |            |      |            |      |            |      |            |
| Male              | 249   | 215        | 251   | 228        | 270   | 252        | 232   | 280        | 250   | 226        | 274   |
| Female            | 240   | 215        | 248   | 230        | 282   | 242        | 217   | 268        | 243   | 217        | 271   |
| Total             | 245   | 215        | 250   | 228        | 274   | 245        | 218   | 271        | 247   | 218        | 272   |
| Macular Thickness (μm) |      |            |      |            |      |            |      |            |
| Male              | 278   | 255        | 277   | 262        | 302   | 276        | 258   | 291        | 277   | 257        | 298   |
| Female            | 279   | 260        | 278   | 255        | 303   | 276        | 253   | 292        | 277   | 255        | 297   |
| Total             | 278   | 257        | 277   | 256        | 302   | 276        | 258   | 291        | 277   | 256        | 297   |

(Continued)
Discussion
Optical coherence tomography has become an established and indispensable method for the diagnosis and monitoring of many retinal and optic nerve diseases in the pediatric population, however the technique is still underutilized in this population because of expected difficulties when performing the test and more importantly, lack of normative database.2

Table 2 (Continued).

| Macular Parameters | Age Group (Years) | <10 | 10–12 | >12 | Total |
|--------------------|------------------|-----|-------|-----|-------|
|                    | Mean Percentile  | Mean Percentile | Mean Percentile | Mean Percentile | Mean Percentile |
|                    | 5th 95th         | 5th 95th         | 5th 95th         | 5th 95th         | 5th 95th         |
| Inner circle       |                  |                  |                  |                  |                  |
| Superior (μm)      | Male             | 321 294 346     | 318 302 341     | 317 296 341     | 319 294 345     |
|                    | Female           | 318 298 342     | 319 290 341     | 314 295 346     | 317 295 346     |
|                    | Total            | 320 294 346     | 319 293 341     | 315 296 341     | 318 295 345     |
| Superior (μm)      | Male             | 318 287 342     | 315 294 345     | 318 300 338     | 317 291 342     |
|                    | Female           | 314 286 337     | 315 292 339     | 310 285 342     | 313 285 340     |
|                    | Total            | 316 287 340     | 315 292 345     | 313 290 338     | 315 291 340     |
| Superior (μm)      | Male             | 321 292 347     | 318 296 344     | 322 302 341     | 320 294 344     |
|                    | Female           | 315 287 339     | 319 295 339     | 314 295 348     | 316 294 345     |
|                    | Total            | 319 292 344     | 319 295 344     | 316 296 345     | 318 294 344     |
| Inferior (μm)      | Male             | 309 281 337     | 306 286 338     | 307 289 328     | 307 284 337     |
|                    | Female           | 302 278 327     | 306 280 338     | 299 275 326     | 302 275 326     |
|                    | Total            | 306 281 336     | 306 280 338     | 301 276 326     | 304 280 333     |
| Nasal (μm)         | Male             | 276 253 300     | 275 260 297     | 271 251 289     | 275 254 297     |
|                    | Female           | 278 256 296     | 276 249 305     | 276 259 292     | 276 250 298     |
|                    | Total            | 277 254 298     | 276 250 303     | 274 257 292     | 276 252 297     |
| Nasal (μm)         | Male             | 271 247 294     | 270 249 298     | 268 251 282     | 270 249 294     |
|                    | Female           | 275 256 314     | 267 242 293     | 268 247 286     | 270 246 294     |
|                    | Total            | 273 249 301     | 269 246 298     | 268 247 285     | 270 247 294     |
| Temporal (μm)      | Male             | 294 269 315     | 293 275 318     | 290 267 307     | 293 270 316     |
|                    | Female           | 297 277 319     | 297 264 328     | 293 274 319     | 296 267 321     |
|                    | Total            | 295 270 316     | 295 266 327     | 292 272 316     | 294 270 319     |
| Temporal (μm)      | Male             | 262 239 284     | 259 241 284     | 258 239 283     | 260 239 284     |
|                    | Female           | 262 239 279     | 259 240 282     | 257 236 273     | 259 239 280     |
|                    | Total            | 262 239 283     | 259 240 284     | 257 239 273     | 259 239 283     |

Abbreviation: CST, central subfield thickness.
Table 3 Multivariate Analysis of the Association Between Macular Measurements and Sex, Age, and Spherical Equivalent Refraction

| Regression Coefficient (B) | 95% Confidence Interval | P-value |
|----------------------------|-------------------------|---------|
|                             | Lower Bound             | Upper Bound |
| Macular volume             |                         |          |
| Sex (male vs female)       | 0.00                    | −0.15    | 0.15    | 0.983 |
| Age (Years)                | 0.00                    | −0.03    | 0.03    | 0.985 |
| SER                        | 0.07                    | 0.03     | 0.11    | 0.002 |
| CST                        |                         |          |
| Sex (male vs female)       | 7.62                    | 2.06     | 13.17   | 0.008 |
| Age (Years)                | 0.47                    | −0.49    | 1.44    | 0.335 |
| SER                        | 0.40                    | −1.24    | 2.03    | 0.632 |
| Average macular thickness  |                         |          |
| Sex (male vs female)       | −0.24                   | −4.35    | 3.87    | 0.909 |
| Age (Years)                | 0.01                    | −0.71    | 0.72    | 0.985 |
| SER                        | 1.96                    | 0.75     | 3.17    | 0.002 |

Inner macular ring

| Superior                   | Sex (male vs female) 2.27 | −2.63 | 7.18 | 0.361 |
|                           | Age (Years) −0.11         | −0.96 | 0.75 | 0.807 |
|                           | SER 2.19                 | 0.74  | 3.63 | 0.003 |
| Inferior                  | Sex (male vs female) 4.45 | −0.63 | 9.53 | 0.085 |
|                           | Age (Years) 0.15          | −0.73 | 1.04 | 0.729 |
|                           | SER 1.91                 | 0.42  | 3.41 | 0.013 |
| Nasal                     | Sex (male vs female) 4.66 | −0.53 | 9.84 | 0.078 |
|                           | Age (Years) 0.32          | −0.58 | 1.22 | 0.488 |
|                           | SER 1.89                 | 0.36  | 3.41 | 0.016 |
| Temporal                  | Sex (male vs female) 4.94 | −0.15 | 10.03| 0.057 |
|                           | Age (Years) −0.12         | −1.00 | 0.77 | 0.792 |
|                           | SER 1.62                 | 0.12  | 3.12 | 0.035 |

Outer macular ring

| Superior                   | Sex (male vs female) −1.98 | −6.26 | 2.31 | 0.363 |
|                           | Age (Years) −0.04          | −0.78 | 0.71 | 0.923 |
|                           | SER 2.64                  | 1.38  | 3.90 | 0.000 |
| Inferior                  | Sex (male vs female) −0.05 | −4.80 | 4.71 | 0.984 |
|                           | Age (Years) −0.47          | −1.29 | 0.36 | 0.267 |
|                           | SER 1.79                  | 0.39  | 3.19 | 0.013 |

(Continued)
Although OCT in children proved to be repeatable and reproducible, normative data are still not provided by the OCT manufacturers in their machines for subjects younger than 18 years, and therefore, the provision of such data is still a necessity.

The current study reported the normative data for macular thickness and macular volume in a sample of healthy Middle Eastern children from Jordan and examined the effect of sex, age, and refractive errors on these data.

In the current study, the mean of macular average thickness was 277.2±12.5 μm, and the mean of the central subfield thickness was 246.7±16.8 μm. Those measurements were comparable to those reported by studies that used the Cirrus SD-OCT, which ranged from 271 μm to 289 μm for the macular average thickness, and from 235 μm to 255 μm for the central subfield thickness. In particular, our results for the macular average thickness and CST were very close to those reported by Al-Haddad (279.6±12.5 μm, 249.1±20.2 μm, respectively) in the only study performed using Cirrus SD-OCT on a sample of

| Table 3 (Continued). |
|----------------------|
|                        | Regression Coefficient (B) | 95% Confidence Interval | P-value |
|                        |                             | Lower Bound | Upper Bound |
| Nasal                  | Sex (male vs female)        | −3.22       | −8.21       | 1.77 | 0.204 |
|                        | Age (Years)                 | −0.17       | −1.04       | 0.69 | 0.695 |
|                        | SER                         | 1.83        | 0.36        | 3.30 | 0.015 |
| Temporal               | Sex (male vs female)        | 0.90        | −3.33       | 5.13 | 0.674 |
|                        | Age (Years)                 | −0.18       | −0.91       | 0.56 | 0.633 |
|                        | SER                         | 2.55        | 1.30        | 3.79 | 0.000 |

**Abbreviations:** SER, spherical equivalent refraction. CST, central subfield thickness.

| Table 4 | Sex, Age, and Spherical Equivalent Refraction Adjusted Means of All Macular Parameters |
|---------|----------------------------------------------------------------------------------------|
| Macular Parameter | Mean* | SE   | 95% Confidence Interval |
|                        |       |      | Lower Bound | Upper Bound |
| Macular volume (mm³)   | 9.978 | 0.037 | 9.906 | 10.051 |
| CST (μm)               | 246.871 | 1.376 | 244.150 | 249.592 |
| Average macular thickness (μm) | 277.202 | 1.018 | 275.190 | 279.214 |
| Inner circle (μm)      |       |      |            |            |
| Superior               | 317.973 | 1.215 | 315.571 | 320.375 |
| Inferior               | 314.846 | 1.259 | 312.357 | 317.335 |
| Nasal                  | 317.977 | 1.285 | 315.437 | 320.517 |
| Temporal               | 304.484 | 1.262 | 301.990 | 306.979 |
| Outer circle (μm)      |       |      |            |            |
| Superior               | 275.584 | 1.062 | 273.485 | 277.683 |
| Inferior               | 269.818 | 1.178 | 267.489 | 272.147 |
| Nasal                  | 294.070 | 1.235 | 291.628 | 296.513 |
| Temporal               | 259.310 | 1.047 | 257.239 | 261.380 |

**Note:** *Adjusted for age, spherical equivalent refraction, and sex.

**Abbreviations:** SE, standard error of the mean. CST, central subfield thickness.
Middle Eastern children from Lebanon, with nearly similar age distribution (10.7±3.1 years). Similarly, the means of the inner and outer ETDRS grid quadrants from the current study were comparable to those from the other studies using Cirrus SD-OCT. 3,8-13 Although OCT measurements from different machines cannot be used interchangeably, the Primus SD-OCT machine used in the current study and the Cirrus SD-OCT are both made by the same manufacturer, use the same technology, and both machines provided very similar mean values of macular parameters when a comparative analysis was performed for both machines. 5 The average macular thickness and CST were found to be less in general when compared to those reported by studies conducted using the Spectralis SD-OCT, 14-18 which is known to give higher values due to different measurement algorithms and software used in different machines. 19 It is important to note that the value of comparisons between the current study’s results and those of other research may be limited by the influence of age range, refractive error state, type and size of the studied sample, ethnicity, and methodology.

Regarding age, the current study sample involved a wide range of ages but excluded those younger than 6 years for the expected lack of cooperation. We did not find a significant association between age and the measured macular parameters, in line with several previous reports. 12,14,20-24 However, other studies reported a relation between age and the following: CST, 8,9,11,15,17,18,25 specific segmented retinal layers, 26-28 macular volume, 17,18 all macular parameters, 3,13 and CST in black but not white children. 29 These results are variable regarding the measured anatomical area and therefore, cannot be generalized. A longitudinal study design would be preferable for establishing a relationship between age and macular characteristics.

We found a significantly higher CST in boys than girls, but other macular parameters showed no sex difference. Many studies reported a sex difference particularly in CST, with males showing higher values than females, 3,4,8-11,13,21 while other studies reported no difference, and we found no reports showing higher values in females regarding macular parameters. This sex difference is also noted in the adult population, 30,31 however Wexler 31 found that this sex difference became non-significant in subjects older than 43 years and suggested that sex difference in the younger adults (<43 years) is due to gonadal hormonal effect.

The spherical equivalent refractive (SER) error was positively correlated with all the macular parameters measured in this study but showed no correlation with the CST. The results of association between SER and macular parameters from previous research are variable. While positive correlation was reported between SER and various macular parameters in several studies, 3,10,13,18,21,32,33 it is interesting to note that all of these studies, except the study by Huynh et al 32 showed either a negative correlation 10,13,21,33 or no correlation with the CST. 3,18 Additionally, several authors 4,8,12,14,16,17 reported no association between SER and any of the measured macular parameters, including the CST. It is still unclear why the CST remains normal or even thicker with smaller SER, but the explanation by Wakitani 34 seems a plausible one, in which decreased peripheral retinal thickness in myopia may act as a compensatory mechanism to preserve central macular thickness.

The current study has a limitation in that it is single-center, clinic-based rather than multi-center, hospital-based design which would reduce selection bias. Another limitation is that ocular axial length was not measured, and therefore the effect of axial length and ocular magnification could not be assessed.

**Conclusion**

The current study presented normative data on macular thickness measurements in healthy Jordanian children aged 6–16 years using SD-OCT. In general, these data were comparable to those from the Middle East, and other regions internationally. The effect of age and refraction needs to be further assessed by longitudinal studies as both factors continuously change with time. Finally, we recommend that OCT manufacturers include normative database in their OCT machines through carefully designed, international multicenter studies.

**Data Sharing Statement**

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.
Ethics Approval and Informed Consent
The study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Review Board at the Jordan University of Science and Technology (Reference number 26-140-2021). Informed consent was obtained from all subjects (guardians) involved in the study.

Author Contributions
All authors made a significant contribution to the conception, study design, execution, acquisition of data, analysis and interpretation; took part in drafting, revising and critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Disclosure
The authors report no conflicts of interest in this work.

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