Abstract. The aim of the present study was to evaluate the accuracy of the Topcon 3D optical coherence tomography (OCT)-2000 built-in algorithm in analyzing OCT data acquired using the Topcon 3D OCT-1000 instrument. Raw data of 3D macular 512x128 scans acquired using the Topcon 3D OCT-1000 instrument were analyzed using the Topcon 3D OCT-2000. The occurrence and severity of segmentation error (SE) were compared between the built-in algorithms of the two instruments. Agreement in retinal thickness measurement between the two systems was evaluated in normal and abnormal eyes. A total of 87 eyes from 87 patients were included. The image quality score evaluated by Topcon OCT-2000 software was lower than that of OCT-1000. No statistically significant difference was identified in the SE rate (77.01 vs. 74.71%; P=0.864) or mean SE score (15.97 vs. 16.30; P=0.763) of the total scan area between the two algorithms. Intraclass correlation coefficient values for retinal thickness were high (0.951-0.995). The mean paired difference in retinal thickness was 3.72-5.77 µm (P<0.05) in normal and 0.61-9.52 µm (P<0.05) in abnormal eyes. No significant difference in retinal segmentation performance was identified between OCT-2000 and OCT-1000 when analyzing OCT-1000 raw data. In conclusion, retinal thickness measurements analyzed by the two OCT algorithms may be used interchangeably in normal eyes. Abnormal eyes required investigations as big differences in retinal thickness measurements may occur due to severe SEs.

Introduction

In the last few years, optical coherence tomography (OCT) has served as an important method for the diagnosis and follow-up of retinal diseases (1). It has also been increasingly used in demonstrating retinal and optic nerve damage in patients with neurological disorders, including multiple sclerosis (2-4) and neuromyelitis optica (5). The application of Fourier transform techniques in spectral domain OCT allows for simultaneous measurements of light reflex from different layers, thus improving image acquisition speed (6). However, certain spectral domain OCT models are still facing certain challenges (7), one of which is the balancing of scan time reduction and image quality. Higher pixel density requires a longer image acquisition time. Elderly patients with Parkinson's disease (8) or severe eye diseases may not be able to cooperate well during the measurements and are more prone to generating motion artifacts. Low data processing speed may be another issue faced in busy clinics in China treating a high volume of patients.

With the advancement of imaging technology, a series of OCT devices have been released and the above-mentioned issues have been improved to a certain extent. Introduced after the initial model Topcon 3D OCT-1000, Topcon 3D OCT-2000 is one of the updated, commercially available OCT instruments from Topcon. According to the manual (9), compared to the 18,000 A scans/sec by Topcon 3D OCT-1000, the enhanced 27,000-50,000 A scans/sec by the OCT-2000 series allow for faster tomography acquisition and minimize artifacts generated by eye movement. The computation time of OCT-2000 for data processing is ~30 sec, while that of OCT-1000 is ~90 sec. With the development of additional noise reduction and enhanced depth (2.3 vs. 1.68 mm) by built-in imaging software, OCT-2000 provides better visualization of the retina and choroid than OCT-1000. The combination of OCT scan and retinal angiography in OCT-2000 allows for accurate positioning and facilitates the exploration of disease pathogenesis. OCT-2000 is a better choice in clinical settings where time and space is limited. As the replacement of OCT-1000 by OCT-2000 has become increasingly widespread, it is important to deal with patient data acquired using OCT-1000. Although Topcon 3D OCT-2000 allows import and re-analysis of raw data from 3D OCT-1000, the performance remains elusive and requires to be evaluated.
The purpose of the present study was to investigate the reliability of the re-analysis of 3D OCT-1000 data by built-in algorithm of 3D OCT-2000. The segmentation error (SE) rate and severity were compared by evaluating each cross-sectional image for each case and assessing the agreement of retinal thickness measurement between the two algorithms. Particular attention was paid to the central subfield, as it is the most important location associated with visual acuity.

**Patients and methods**

**Study subjects.** The present study was approved by the Institutional Review Board of the Joint Shantou International Eye Center (JSIEC) of Shantou University and the Chinese University of Hong Kong (Shantou, China), and followed the tenets of the Declaration of Helsinki. Informed consent was not required from subjects due to the retrospective nature of the study.

Patients who had complete electronic records in the JSIEC, including information regarding visual acuity, non-contact tonometry, slit-lamp biomicroscopy and fundus examination, and who were examined using Topcon 3D OCT-1000 with an image quality of ≥50 were included in the present study. All medical records, including the diagnosis of these patients, were retrospectively reviewed. Normal subjects and a variety of patients with retinal disorders were included. The criteria of ‘normal’ included: i) No history of retinal disease or glaucoma; and ii) the retinal structure was normal on fundus examination and OCT scan. The exclusion criteria of OCT images included: i) Distorted image caused by motion artifacts; and ii) incomplete image caused by long axial length or severe opacity changes along the visual axis. In subjects who had received an OCT scan in the bilateral eyes, only one eye was randomly selected for assessment. All images were obtained using the 3D macular 512x128 scan mode (128 B-scans in total, each B-scan consisting of 512 A-scans, covering an area of 6x6 mm²) on a Topcon 3D OCT-1000 machine (software version 2.20). The raw data was exported from the OCT-1000 in ‘.fds’ format and imported to an OCT-2000 machine (software version 8.11.003.04) for re-analysis. The built-in algorithms of OCT-1000 and OCT-2000 instruments analyzed the raw data automatically.

**SE and thickness measurement.** SE assessment in the two algorithms was performed by a blinded investigator (BC). SE was defined as the disagreement between automatic and manual identification of the inner and outer retinal boundaries. The inner and outer boundaries refer to the anterior border of the internal limiting membrane and the anterior border of retinal pigment epithelium (RPE), respectively (11). Full-thickness macular hole (MH) was defined at a center thickness of 0 µm, in which the inner border overlapped with the outer border (12).

The severity of SE in the anterior and posterior borders of each B-scan was evaluated by a graded scale described by Sadda et al (13), which has also been validated in other studies (14-17). The criteria were the following: i) Any deviation that may be recognized from the actual boundary was given 1 point; ii) to emphasize the importance of foveal measurements in clinical diagnosis and study, 1 additional point was given if the deviation was located within the central subfield, which was defined as the central 1-mm area of the macula; iii) 1 point was added when an SE or sum of multiple discontinuous errors appeared to be longer than 1 mm. If the error/sum of errors was longer than 3 mm, another point was given; iv) in axial dimension, 1 point was added for a deviation larger than one third of the actual retinal thickness and 2 points were given when the deviation increased to more than two thirds of the retina. The total SE score was calculated by adding all SE points from the inner and outer boundaries of each cross section (128 B scans in total). The SE score of the central subfield was further analyzed.

The built-in software of Topcon OCT assumes foveal fixation and generates an Early Treatment of Diabetic Retinopathy Study (ETDRS) thickness map centered on this location. The ETDRS plot includes three circles with diameters of 1, 3 and 6 mm, dividing the macula into two rings. It is further divided into four quadrants: Superior, inferior, nasal and temporal. Retinal thickness given by the two algorithms was compared without correction in each subfield of the ETDRS map, without adjustment of center location and retinal boundaries.

**Statistical analysis.** The difference in image quality score as assessed by the two algorithms was evaluated using a Student's paired t-test and Pearson's correlation. The presence of SEs was compared between normal and abnormal eyes using a Chi-square test, and between OCT-1000 and OCT-2000 using McNemar's test. The independent-samples t-test was used to compare the image quality score between groups with and without SEs, and compare the SE score between normal and abnormal eyes. Intraclass Correlation Coefficient (ICC) analysis and a Student's paired t-test were used to analyze the correlation and difference in thickness measurement between the two algorithms, respectively. Bland-Altman plots were used to evaluate the agreement between the two algorithms. SPSS statistical software (version 18.0.0; SPSS, Inc.) was used to perform the statistical analysis and draw a scatter plot. MedCalc software (version 15.2.2; MedCalc Software) was used to draw Bland-Altman plots.

**Results**

**Patient characteristics.** A total of 87 eyes from 87 patients, including 41 (47.13%) male and 46 (52.87%) female subjects, were included in the present study. The mean age of the patients was 44.08±15.12 years. Among the eyes included, 43 (49.43%) were normal and 44 (50.57%) were abnormal. The diagnoses of abnormal eyes included central serous choriorretinopathy (36.36%), retinal vascular diseases (18.18%), age-associated macular degeneration (AMD) (15.91%), MH (6.82%) and other retinal diseases (22.73%). The image quality score re-assessed by the 3D OCT-2000 algorithm was significantly lower than the original score determined by the 3D OCT-1000 algorithm, with a mean difference of 19.18±1.87 (P<0.001; paired t-test). A highly linear correlation between the image quality scores of the OCT-1000 and OCT-2000 algorithms was identified (r=0.994, P<0.001; Fig. 1).

**Comparison of SE rate and score.** SEs were present in normal as well as abnormal cases, but were more frequent in abnormal ones (Table 1). All cases of MH and AMD with
Comparison of retinal thickness measurements. Retinal thickness measured by the two algorithms was highly correlated \([r, 0.987-0.999\) (all \(P<0.001\); ICC, 0.951-0.995] in all ETDRS regions for the normal and abnormal eyes (Table III). The thickness was greater when assessed by OCT-2000 than by OCT-1000 in all ETDRS regions for normal and abnormal subjects, except in the inferior inner region of abnormal subjects. The difference in thickness between the two algorithms, was 0-11 \(\mu m\) in normal and 0-85 \(\mu m\) (case with MH) in abnormal group, respectively. The mean difference was 3.72-5.77 \(\mu m\) in the normal and 0.61-9.52 \(\mu m\) in the abnormal group, respectively (Table III; Fig. 3). It was also indicated that the 95% confidence interval for the difference was relatively smaller in the normal group (Fig. 3).

Discussion

In the present study, the raw data acquired with an OCT-1000 instrument were analyzed using OCT-1000 and OCT-2000 algorithms and their performance and results were compared. It was revealed that the SE rate and SE score were similar between the two algorithms in the entire scan region. However, in the central subfield, the OCT-2000 algorithm performed worse than the OCT-1000 algorithm, with a higher SE score. The retinal thickness measurements were highly correlated between the two algorithms. The thickness measurements obtained with OCT-2000 were larger than those obtained with OCT-1000 by several microns.

Previous studies have demonstrated that the incidence of SE and discrepancy between different OCTs was associated with imaging technology, as well as the segmentation algorithm (18,19). Kim et al (15) investigated the accuracy of the Topcon 3D OCT-1000 algorithm in analyzing Stratus OCT data and revealed that the OCT-1000 algorithm performed better than Stratus OCT in segmentation. In the present study, OCT-2000 failed to perform better than OCT-1000 in analyzing data acquired with OCT-1000. Even in the central subfield, the OCT-2000 algorithm performed worse than the OCT-1000 algorithm. One possible reason may be the lower image quality score for OCT-2000. Following re-analysis, the image quality clearly decreased to 33-47. According to Falavarjani et al (20), lower image quality led to a higher SE rate in normal eyes and eyes with clinically significant macular edema. Since a higher image quality may increase the sharpness of the retinal boundary (21) and thus decrease the SE rate, the OCT-2000 system may become less sensitive to the retinal boundary with poor image quality. However, with the narrow range in the level of image quality (only 33-47), it was not possible to demonstrate that a higher image score leads to a better segmentation performance. Further research is required to elucidate the effect of image quality on SE.

The differences in thickness were statistically significant, with OCT-2000 always overestimating retinal thickness as compared to OCT-1000. The highest mean difference of the 9 ETDRS areas located in the central subfield was 5.77 \(\mu m\) in the normal and 9.52 \(\mu m\) in the abnormal group. The systemic difference may be due to differences in built-in software algorithms in the two OCT devices (22), various degree of misinterpretation of the double contoured RPE choriocapillaris band (23) in Topcon OCT-1000 and misidentification of ILM in Topcon OCT-2000. Another reason may be the alteration of the ETDRS map location. Odell et al (24) compared the ETDRS plot centered at the
location detected by Cirrus HD-OCT with the plot centered at the fovea and determined that the two plots differed by 14.4 µm on average, reaching 100 µm (sum of difference in all ETDRS subfields) in normal eyes and even higher in diseased eyes. Although internal fixation was used with the Topcon OCT-1000 when scanning eyes, certain aged and abnormal cases may not be able to sufficiently cooperate, leading to errant fixation (25). The auto fovea function in the OCT-2000 algorithm may help in the search for the foveal center, while the OCT-1000 does not have this function. Therefore, the ETDRS map location may be different between the two algorithms, causing a difference in the thickness determined (Fig. 4). However, correlation analysis and ICC values indicated a considerable agreement between

Table I. Comparison of segmentation error rate between Topcon 3D OCT-1000 and Topcon 3D OCT-2000 algorithms in analyzing OCT raw data captured with Topcon OCT-1000.

| Region                  | N     | Number of eyes with segmentation error | P-valuea          |
|-------------------------|-------|----------------------------------------|-------------------|
|                         |       | 3D OCT-1000 | 3D OCT-2000 |                  |
| Entire scan region      |       |             |             |                  |
| Normal eyes             | 43    | 31 (72.09) | 31 (72.09) | 0.999            |
| Abnormal eyes           | 44    | 36 (81.82) | 34 (77.27) | 0.791            |
| Total                   | 87    | 67 (77.01) | 65 (74.71) | 0.864            |
| Central subfield        |       |             |             |                  |
| Normal eyes             | 43    | 2 (4.65)   | 5 (11.63)  | 0.453            |
| Abnormal eyes           | 44    | 15 (34.09) | 17 (38.64) | 0.625            |
| Total                   | 87    | 17 (19.54) | 22 (25.29) | 0.227            |

The raw data was exported from the OCT-1000 and imported to an OCT-2000 machine for re-analysis. Values are expressed as n (%). aP-values for comparing the segmentation error rate between the two algorithms were calculated using the McNemar test. b,cP-values for comparing the segmentation error rate between normal and abnormal eyes in entire scan region and central subfield, respectively, were calculated using the Chi-square test. OCT, optical coherence tomography.

Figure 2. Representative cases with SEs on Topcon OCT-1000 (left-hand panel) and OCT-2000 (right-hand panel. (A and B) A case of a full-thickness macular hole with SE on OCT-1000 and OCT-2000. The segmentation line of the inner retinal boundary directly extends between the two edges and produces a thickness map without any obvious decrease in retinal thickness in both OCT algorithms. (C and D) An AMD case with misidentification of the outer retinal border on OCT-1000 and OCT-2000. (E and F) A normal subject with misinterpretation of the outer retina border by OCT-1000 but not OCT-2000. (G and H) Normal subject with misidentification of the inner border and overestimation of the retinal thickness by OCT-2000 but not OCT-1000. SE, segmentation error; OCT, optical coherence tomography; AMD, age-associated macular degeneration.
According to the Bland-Altman plots, the amount of dissimilarity was just a few microns in the normal group. The difference was insignificant and indicated that retinal thickness measurements analyzed by the two OCT built-in algorithms may be used interchangeably in normal cases. In the abnormal group, the discrepancy ranged from 0 to 85 with various SEs. Therefore, these two measurements should not be used interchangeably prior to excluding severe SEs in disease cases, particularly in subjects with MH and CNV.

Table II. Comparison of SE scores between Topcon 3D OCT-1000 and Topcon 3D OCT-2000 algorithms.

| Region                  | OCT-1000         | OCT-2000         | Difference | P-value\(^a\) |
|-------------------------|------------------|------------------|------------|--------------|
|                         | Normal           | Abnormal         |            |              |
| Entire scan region      |                  |                  |            |              |
| Normal                  | 3.14±4.54 (0-25) | 5.35±6.37 (0-27) | -2.21±8.43 | 0.093        |
| Abnormal                | 28.50±37.32 (0-136) | 27.00±37.02 (0-140) | 1.50±11.58 | 0.395        |
| Total                   | 15.97±29.48 (0-136) | 16.30±28.70 (0-140) | -0.33±10.26 | 0.763        |
|                         | P-value\(^b\)    |                  |            |              |
| Central subfield        |                  |                  |            |              |
| Normal                  | 0.09±0.43 (0-2)  | 0.98±3.19 (0-16) | -0.88±3.25 | 0.081        |
| Abnormal                | 13.59±24.58 (0-95) | 14.57±24.36 (0-95) | -0.98±4.31 | 0.139        |
| Total                   | 6.92±18.66 (0-95) | 7.85±18.67 (0-95) | -0.93±3.80 | 0.025        |
|                         | P-value\(^b\)    |                  |            |              |

Values are expressed as the mean ± standard deviation (range). The \(^a\)-P-value was calculated from a paired t-test comparing the SE scores of the Topcon 3D OCT-1000 and -2000 algorithms. \(^b\)-P-values for comparing the segmentation error rate between normal and abnormal eyes in entire scan region and central subfield, respectively, were calculated using the Chi-square test. OCT, optical coherence tomography; SE, segmentation error.

Table III. Comparison of macular thickness analyzed with 3D-OCT-1000 and -2000 algorithms in normal and abnormal eyes.

| Region                  | OCT-1000         | OCT-2000         | \(r\)      | ICC value | Difference (µm) |
|-------------------------|------------------|------------------|------------|-----------|-----------------|
|                         | Normal           | Abnormal         |            |           |                 |
| Retinal thickness (µm)  |                  |                  |            |           |                 |
| Central                 | 219.67±19.54     | 225.44±19.53     | 0.998\(^a\) | 0.956\(^a\) | -5.77±1.31\(^a\) |
| Superior inner          | 299.09±17.12     | 302.81±17.00     | 0.999\(^a\) | 0.975\(^a\) | -3.72±0.93\(^a\) |
| Nasal inner             | 299.72±19.11     | 303.60±19.46     | 0.999\(^a\) | 0.979\(^a\) | -3.88±0.93\(^a\) |
| Inferior inner          | 284.95±22.59     | 289.14±22.66     | 0.999\(^a\) | 0.983\(^a\) | -4.19±0.73\(^a\) |
| Temporal inner          | 281.35±13.78     | 285.30±13.89     | 0.998\(^a\) | 0.959\(^a\) | -3.95±0.82\(^a\) |
| Superior outer          | 257.86±13.08     | 261.63±13.49     | 0.997\(^a\) | 0.958\(^a\) | -3.77±1.17\(^a\) |
| Nasal outer             | 278.44±18.44     | 282.26±18.66     | 0.999\(^a\) | 0.978\(^a\) | -3.81±0.98\(^a\) |
| Inferior outer          | 256.35±16.03     | 260.19±16.23     | 0.996\(^a\) | 0.969\(^a\) | -3.84±1.38\(^a\) |
| Temporal outer          | 247.02±13.01     | 251.12±13.31     | 0.997\(^a\) | 0.951\(^a\) | -4.09±1.09\(^a\) |
|                         | P-value\(^b\)    |                  |            |           |                 |
| Abnormal                | 270.30±110.20    | 279.82±107.02    | 0.987\(^a\) | 0.983\(^a\) | -9.52±17.58\(^a\) |
| Superior inner          | 315.61±67.63     | 320.89±67.78     | 0.992\(^a\) | 0.990\(^a\) | -5.27±8.32\(^a\) |
| Nasal inner             | 325.93±74.72     | 330.11±75.37     | 0.997\(^a\) | 0.995\(^a\) | -4.18±5.82\(^a\) |
| Inferior inner          | 314.91±75.37     | 315.52±77.28     | 0.992\(^a\) | 0.992\(^a\) | -0.61±10.01     |
| Temporal inner          | 298.34±61.94     | 303.30±62.56     | 0.998\(^a\) | 0.995\(^a\) | -4.96±3.86\(^a\) |
| Superior outer          | 267.84±34.58     | 269.82±35.10     | 0.992\(^a\) | 0.990\(^a\) | -1.98±4.44\(^a\) |
| Nasal outer             | 284.86±32.98     | 289.36±33.55     | 0.996\(^a\) | 0.987\(^a\) | -4.50±3.09\(^a\) |
| Inferior outer          | 258.48±30.26     | 263.34±30.47     | 0.993\(^a\) | 0.981\(^a\) | -4.86±3.48\(^a\) |
| Temporal outer          | 248.07±25.42     | 251.36±25.60     | 0.993\(^a\) | 0.985\(^a\) | -3.30±3.11\(^a\) |

Values are expressed as the mean ± standard deviation. \(^a\)-P<0.05 of OCT-1000 vs. OCT-2000. R, Correlation coefficient of Pearson’s correlation analysis; ICC, intraclass correlation coefficient; OCT, optical coherence tomography.
In the present study, errors in retinal boundary detection were observed in 77.01% of eyes using the OCT-1000 algorithm and 74.71% using the OCT-2000, a relatively high percentage when compared to previous studies of SE in association with OCT (14,15,26,27). Ray et al (27) reported that retinal thickness measurement errors occurred in 62.2% of the total scan area with a Stratus OCT. In a study that analyzed Stratus data with Topcon 3D OCT viewer, the SE rate was 30.9% (15). Song et al (14) assessed 116 eyes, including normal and abnormal cases, and determined that the SE rate
with the Topcon OCT-1000 was 63.8% in the 12 radial scan mode. Since various study designs were used, different retinal boundary error criteria and different subjects included may explain for the variance in the SE rate. The higher SE rates in the present study may be due to the complete analysis of all 128 cross-section images, since a minor error in any of the 128 images may lead to an SE. In the fast macular protocol of the stratus OCT, only 6 cross-section images were evaluated (15), thus lowering the possibility of SE, even with a ‘relatively low-level algorithm’. Although Song et al (14) scanned eyes using spectral-domain OCT, the presence of SEs in the total scan area was assessed in 12 images, in which the sample density was much lower. The SE rate of the central subfield may be more comparable, since the same scan mode and sample density were used for the evaluation. In the present study, a relatively low central subfield SE rate in the normal and abnormal groups was obtained for the two OCT algorithms, as compared with those in the study by Song et al (14) (22.5% for normal subjects, 68.9% for the retinal pathology group and 83.9% for the subretinal pathology group). Possible explanations include the lower percentage and severity of abnormal eyes included, as well as a more recent software version and different criteria used to assess SEs in the present study.

It is not a surprise that the abnormal group had a higher SE rate than the normal group, since OCT segmentation algorithms were designed based on normal data. Diseases may affect the characteristics of retinal interface and cause misidentification (28,29). In the present study, the SE score was considerably lower in the normal group, in the central as well as the total scan areas, for the assessment by either of the two OCT algorithms. According to the study by Song et al (14), SEs were more frequent and severe in the subretinal and retinal pathology groups than in the normal group. Ho et al (30) identified a poor agreement between manual and automated segmentation in eyes with retinal pigment epithelial detachment, as assessed by the Cirrus HD-OCT. The high percentage of misidentification of the inner border in MH and outer border in AMD in the present study also illustrated that disease is an important factor affecting SEs.

Of note, the present study had certain limitations. The image quality of the scan data clearly decreased following re-analysis with OCT-2000. It was not possible to identify the reason for this, since the standards of image quality grading in the two OCT devices were not known to us. However, this may be explained by the higher grading criteria of the OCT-2000, since the same raw data were analyzed. Images with a poor signal in the OCT-1000 may be assigned an extremely low-quality score in the OCT-2000, which may cause severe misidentification of the retinal boundary, illustrating that OCT data obtained with poor scan quality are difficult to accurately re-analyze with an advanced OCT algorithm in the Topcon series. However, this cannot be avoided in a clinical setting, since patients are not always able to cooperate, particularly those with poor vision or media opacity. Another limitation of the present study is that it only focused on the condition of retinal boundary and thickness deviation, regardless of SE determinants. Poor scan acquisition (13) and image artifacts (27) were previously reported to also cause SEs. Due to the retrospective nature of the present study, it was not possible to gather this information as previous studies did. Instead, only the effect of disease and image quality on SE was analyzed. Another limitation was that the present study did not analyze the SE rate and score in different disease groups. Since the abnormal cases included exhibited a wide variation and were difficult to classify, it was not possible to compare the incidence and severity of SE caused by different diseases.

In conclusion, the SEs obtained with the two OCT algorithms were relatively high. The OCT-2000 algorithm did not exhibit a better segmentation performance in the analysis of data acquired with the OCT-1000. It is, however, noteworthy that not all SEs have an equally important effect on clinical diagnosis. In spite of a systemic difference in the measurement of retinal thickness between the two models, with high ICC values and a small amount of dissimilarity, it was still possible to use the measurements interchangeably in normal cases and abnormal cases without SEs.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

MZ and HC conceived and designed the experiments. BC performed the experiments. BC, HC and CZ analyzed the data. BC and HC wrote the paper. BC, HC, CZ and MZ revised the manuscript.

Ethics approval and informed consent

The present study was approved by the Institutional Review Board of the JSIEC of Shantou University and the Chinese University of Hong Kong, and followed the tenets of the Declaration of Helsinki. Informed consent from the subjects was not required due to the retrospective nature of the study.

Patient consent for publication

Not applicable.

Competing interests

None of the authors had any competing interests or financial interests associated with the work presented in this manuscript.
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