Clinical Comparison of Conventional Coaxial Phacoemulsification and Coaxial Microincision Phacoemulsification

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Abstract

Purpose: To compare the outcomes of coaxial microincision phacoemulsification with that of conventional coaxial phacoemulsification

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Methods: In a prospective study, 74 eyes of 74 patients with cataract were randomly selected to have cataract extraction using 1 of 2 techniques: coaxial microincision phacoemulsification through a 2.2 mm incision (37 eyes) or conventional coaxial phacoemulsification through a 2.8 mm incision (37 eyes) and foldable intraocular lens (IOL) (SA60; Alcon) implantation. Intraoperative parameters were effective phacoemulsification time (EPT), surgical time, and total volume of balanced salt solution (BSS) used. Assessed ocular biometrics included corneal topography, to evaluate surgically induced astigmatism (SIA), as well as corneal thickness and endothelial cell count (ECC).

Results: Using vectorial analysis the amount of SIA was 0.04±0.34 diopter (D) at 126.7 degrees in the 2.8 mm group and 0.07±0.49 D at 11.8 degrees in the 2.2 mm group, at one month postoperatively. At 3 months, the SIA was 0.06±0.41 D at 134.7 degrees and 0.10±0.62 at 161.4 degrees in the 2.8 mm and 2.2 mm groups, respectively.

Conclusion: Although coaxial microincision cataract surgery (MICS) was a safe and effective technique there were no clinical or statistically significant differences between 2 techniques in minimizing the effect of incision size on SIA.

Keywords: Coaxial Phacoemulsification, Conventional, Microincision
Introduction
Cataract is the leading cause of visual impairment worldwide. Today, cataract surgery is not simply a procedure to remove the opaque lens, but aims at achieving best possible visual outcome with maximum safety and minimum invasiveness. These goals have created a trend toward a smaller wound from a 10 mm incision used for extra capsular cataract extraction (ECCE) to 2.8 mm-2.2 mm incisions in phacoemulsification that are associated with less surgically induced astigmatism (SIA), better fluidics, faster recovery, and less tissue damage and inflammation. But the question is whether this smaller wound results in significantly better clinical results?

A recent study of human cadaver eyes showed better wound architecture in 2.2 mm incision in comparison with 2.75 mm incision.1 Another study implicated less endothelial cell loss in 2.2 mm incision than 2.8 mm incision.2 Hence reviewed studies did not considered some important features including SIA, this study was performed to compare the outcomes of conventional coaxial phacoemulsification through 2.8 mm incision with that of microincision coaxial phacoemulsification through 2.2 mm incision.

Methods
In a prospective double masked randomized clinical trial, 74 eyes of 74 patients were enrolled to undergo phacoemulsification. After explaining the study, surgical procedures, and possible complications, an informed consent was obtained and patients were randomly allocated to the 2.2 mm or 2.8 mm groups. The study proposal was approved by the review board of Noor Ophthalmology Research Center.

Inclusion criteria included senile cataract, no history of ocular surgery, central corneal clarity, at least 7 mm pharmacological pupillary dilation in preoperative examination, normal fundus examination and an endothelial cell count (ECC) of at least 1600 per mm². Exclusion criteria were as follows: astigmatism more than 3.0 diopters (D), potential visual acuity less than 20/40, zonulysis and zonular defects, diabetes mellitus or other known systemic diseases, pupillary anomaly or posterior synechiae, glaucoma, optic atrophy, ocular tumors, history of ocular surgery or ocular trauma and age younger than 40 years old.

Before surgery, all patients underwent a complete ophthalmic examination including refraction, indirect ophthalmoscopy, ultrasound pachymetry (Nidek US-1800), topography (EyeSys-2000) and ECC measurement (Topcon SP 1000).

From corneal topography maps, we also extracted the simulated keratometry values of the central 3 mm zone as keratometry readings. ECC was measured three times and the mean of the three was used. Intraocular lens (IOL) power calculation was performed (IOLMaster, Zeiss). All evaluations were performed by a single operator. Nucleus density was graded according to Lens Opacity Classification System III (LOCS III).

Follow-up examinations were performed at day one, day three, one month and three months after surgery by an independent ophthalmologist. Uncorrected visual acuity (UCVA) was evaluated on each follow-up session. Best corrected visual acuity (BCVA), refraction and pachymetry were obtained in all follow-up sessions except the first day after surgery. Defocus equivalent (DE) is a better predictor of the visual acuity because of its better correlation with the size of the blurred circle on the retina. It can be calculated using:³

\[
DE = |SE| + \frac{1}{2} |cylinder|
\]

Topography was performed one and three months postoperatively and SIA was calculated using the Holladay¹ 10-step formula and cartesian coordinate conversion. For reporting descriptive data, the double-angle polar plot was used as suggested by Holladay et al.⁴

ECC was measured three months after surgery and endothelial cell loss was calculated as:

Endothelial cell loss = \[\frac{\text{Preoperative ECC} - \text{Postoperative ECC}}{\text{Preoperative ECC}} \times 100\]
**Surgical technique**

All surgeries were performed by the same surgeon (HH) under topical anesthesia after pupillary dilation with tropicamide 1% and phenylephrine hydrochloride 2.5% eye drops. A single planar corneal incision was created. Since the surgeon was right-handed, the incision was deviated inferotemporally on the right eye and superotemporally on the left eye using a 2.8 mm metal tip knife in the conventional coaxial phacoemulsification group and a 2.2 mm metal tip knife in the coaxial microincision phacoemulsification group. A single side port was created 90 degrees away using a 1.2 mm clear cut side port knife (Alcon). The ophthalmic viscoelastic device (OVD) was used in both groups; and a continuous curvilinear capsulorrhexis of approximately 5.0 mm was created using capsulorrhexis forceps. After hydrodissection and hydrodelineation, phacoemulsification was performed.

Settings were adjusted according to nucleus density and horizontal phacochop technique was performed using the Legacy (Alcon surgical Inc.) and continuous ultrasound setting. Cortical material was removed with a silicon irrigation/aspiration (I/A) ultrasleave tip. After filling the anterior chamber (AC) with OVD, a hydrophobic acrylic IOL (Alcon SA60AT; Alcon surgical Inc.) with the recommended injector system was implanted into the eye in the 2.8 mm group by insertion of the complete cartridge tip through the clear corneal incision (CCI). For IOL implantation, cartridge and the wound assisted technique in which the injector tip is just inserted in the outside lip of the wound but not all the way to the eye and the incision itself is used as a guide for insertion of the lens was used in the 2.2 mm group. Finally, OVD was removed with the I/A tip and the wound was hydrated. Surgery time was recorded starting from creating the first corneal incision to the end of stromal wound hydration. The effective phacoemulsification time (EPT) and total volume of balanced salt solution (BSS) used during surgery were recorded. Any case of intraoperative complication or wound burn was recorded as well.

**Results**

Thirty four patients (45.9%) were male and forty patients (54.1%) were female and there was no statistically significant difference between the two groups. Patients preoperative data and nuclear density according to LOCSIII classification are shown in table 1 and table 2, respectively.

**Visual acuity**

The results of UCVA and BCVA testing are summarized in table 3. Mean UCVA and BCVA were not significantly different between the two groups at any follow-up session.

Repeated measures analysis of variance showed that UCVA had a significant change ($P<0.001$) but the trend of change over the follow-up period showed no difference between the two groups ($P=0.73$). Also, there was no significant difference in UCVA between the two groups at any follow-up session ($P=0.29$). This was also true for BCVA ($P<0.001$, $P=0.56$, $P=0.57$, respectively).

**Refraction**

SE refraction at three days, one month and 3 months after surgery are shown in table 3. There was no statistically significant difference in SIA between two groups at any time. In repeated measures analysis of variance, the difference of SE between follow-up sessions was borderline significant ($P=0.06$), but there was no statistically significant difference between groups in follow-up period ($P=0.24$).

DE results are shown in table 3; inter-group differences were not statistically significant.

Using repeated measures analysis of variance, the mean SE refraction in the 2.8 mm group showed a significant change during the follow-up period ($P=0.003$). The SE refraction was stable in the 2.2 mm group ($P=0.44$) and there was no difference in the trend of SE change over the follow-up period ($P=0.21$).

**Corneal pachymetry**

Preoperatively, mean central corneal thickness (CCT) was 528±32 μm and 535±36 μm in the 2.8 mm group and 2.2 mm group, respectively; and the difference (7.0 μm) was not statistically significant ($P=0.35$). The mean postoperative CCT values are shown in table 3.
Repeated measures of analysis of variance showed no statistically significant difference between the trends in the two groups.

Comparison of CCT readings with baseline values demonstrated significant differences only with day 3 after surgery in both groups. The thickness reached baseline measures one month after surgery (P=0.85).

**Endothelial cell density**
The mean ECC before surgery was 2582±277 cell/mm² in the 2.8 mm group and 2518±337 cell/mm² in the 2.2 mm group and the difference (63 cell/mm²) was not statistically significant (P=0.38). Mean endothelial cell loss in the 2.8 mm group and the 2.2 mm group 3 months after surgery was 6.52±7.52% and 10.09±9.28%, respectively and the inter-group difference was not statistically significant (P=0.07). After each group was adjusted for the LOCS III grade, there was still no statistically significant difference between the two groups (P=0.9).

**Surgery time**
Mean surgery time was 8.4±2.0 min and 8.6±1.8 min in the 2.8 mm and 2.2 mm group, respectively, with no statistically significant difference between the two groups (P=0.6).

**Effective phacoemulsification time**
Mean EPT was 17.8±13.4 sec and 14.5±10.4 sec in the 2.8 mm and 2.2 mm incision group, respectively, and the difference (3.2 sec) between the two groups was not statistically significant (P=0.2); however, it highly correlated with the LOCS III grade (P<0.001). After adjusting EPT for the LOCS III grade, there was still no difference between the two groups (P=0.32).

**Balanced salt solution**
The mean amount of BSS used during surgery was 148±55 ml in the 2.8 mm group and 138±66 ml in the 2.2 mm group, with no statistically significant difference between the two groups (P=0.49).

**Surgically induced astigmatism**
*Polar plot representation*
The aggregate data of SIA one and three months after surgery are illustrated in double angle polar plots (Figure 1). The centroid of SIA was 0.04±0.34 D at 126.7 degrees in the 2.8 mm group and 0.07±0.49 D at 11.8 degrees in the 2.2 mm group, one month after surgery.

Three months after surgery, the mean SIA was 0.06±0.41 D at 134.7 degrees in the 2.8 mm group and 0.10±0.62 at 161.4 degrees in the 2.2 mm group.

The effects of wound location and wound size on the amount of SIA are shown in figure 2 and figure 3. One month after surgery, mean centroid in the 2.8 mm and 2.2 mm group was 0.06±0.40 D at 196.6 degrees and 0.26±0.49 D at 33.8 degrees, respectively, in the right eyes. In the left eyes, these figures were 0.05±0.34 D at 150.9 degrees and 0.12±0.44 D at 158.4 degrees, respectively.

Three months after surgery, the mean centroid of the aggregation of SIA in the 2.8 mm and 2.2 mm group was respectively 0.13±0.54 D at 140.1 degrees and 0.14±0.33 D at 32.5 degrees in the right eyes, and 0.03±0.26 D at 85.8 degrees and 0.10±0.46 D at 148.1 degrees, in the left eyes.

<table>
<thead>
<tr>
<th>Table 1. Patients’ preoperative data</th>
<th>2.8 mm group</th>
<th>2.2 mm group</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>67.1±11.1</td>
<td>66.5±12.0</td>
<td>0.828</td>
</tr>
<tr>
<td>Endothelial cell count (cell/mm²)</td>
<td>2582±277</td>
<td>2518±237</td>
<td>0.381</td>
</tr>
<tr>
<td>Spherical equivalent (D)</td>
<td>-2.05±3.52</td>
<td>-1.33±2.6</td>
<td>0.102</td>
</tr>
<tr>
<td>UCVA (logMAR)</td>
<td>0.88±0.38</td>
<td>0.79±0.47</td>
<td>0.375</td>
</tr>
<tr>
<td>BCVA (logMAR)</td>
<td>0.52±0.32</td>
<td>0.54±0.42</td>
<td>0.826</td>
</tr>
<tr>
<td>Pachymetry (μm)</td>
<td>528±32</td>
<td>535±36</td>
<td>0.353</td>
</tr>
<tr>
<td>Corneal astigmatism (D)</td>
<td>0.78±0.63</td>
<td>0.80±0.63</td>
<td>0.861</td>
</tr>
</tbody>
</table>

D: Diopter
UCVA: Uncorrected visual acuity
BCVA: Best corrected visual acuity
Table 2. Distribution of lens opacity according to the lens opacity classification system III in each group

<table>
<thead>
<tr>
<th>LOCS III grade</th>
<th>2.8 mm group</th>
<th>2.2 mm group</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>3</td>
<td>6</td>
<td>11</td>
</tr>
<tr>
<td>4</td>
<td>15</td>
<td>16</td>
</tr>
<tr>
<td>5</td>
<td>9</td>
<td>9</td>
</tr>
<tr>
<td>6</td>
<td>4</td>
<td>2</td>
</tr>
</tbody>
</table>

LOCS: Lens opacity classification system

Table 3. Postoperative outcomes in the two groups

<table>
<thead>
<tr>
<th></th>
<th>2.8 mm group (Mean±SD)</th>
<th>2.2 mm group (Mean±SD)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>UCVA (logMAR)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1st day</td>
<td>0.27±0.19</td>
<td>0.26±0.34</td>
<td>0.93</td>
</tr>
<tr>
<td>3rd day</td>
<td>0.17±0.16</td>
<td>0.24±0.32</td>
<td>0.21</td>
</tr>
<tr>
<td>1st month</td>
<td>0.09±0.17</td>
<td>0.13±0.18</td>
<td>0.35</td>
</tr>
<tr>
<td>3rd month</td>
<td>0.11±0.13</td>
<td>0.16±0.22</td>
<td>0.25</td>
</tr>
<tr>
<td>BCVA (logMAR)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3rd day</td>
<td>0.04±0.17</td>
<td>0.09±0.13</td>
<td>0.14</td>
</tr>
<tr>
<td>1st month</td>
<td>0.05±0.08</td>
<td>0.04±0.08</td>
<td>0.51</td>
</tr>
<tr>
<td>3rd month</td>
<td>0.03±0.07</td>
<td>0.04±0.08</td>
<td>0.89</td>
</tr>
<tr>
<td>Spherical equivalent (D)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3rd day</td>
<td>-0.42±0.71</td>
<td>-0.51±0.90</td>
<td>0.6</td>
</tr>
<tr>
<td>1st month</td>
<td>-0.14±0.50</td>
<td>-0.41±0.79</td>
<td>0.09</td>
</tr>
<tr>
<td>3rd month</td>
<td>-0.42±0.53</td>
<td>-0.40±0.76</td>
<td>0.8</td>
</tr>
<tr>
<td>Defocus equivalent (D)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3rd day</td>
<td>1.01±0.86</td>
<td>1.31±1.46</td>
<td>0.291</td>
</tr>
<tr>
<td>1st month</td>
<td>0.81±0.50</td>
<td>1.01±0.81</td>
<td>0.235</td>
</tr>
<tr>
<td>3rd month</td>
<td>0.98±0.59</td>
<td>1.10±0.81</td>
<td>0.479</td>
</tr>
<tr>
<td>Pachymetry (μm)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3rd day</td>
<td>565±38</td>
<td>567±45</td>
<td>0.84</td>
</tr>
<tr>
<td>1st month</td>
<td>535±28</td>
<td>525±86</td>
<td>0.5</td>
</tr>
<tr>
<td>3rd month</td>
<td>531±29</td>
<td>533±37</td>
<td>0.82</td>
</tr>
</tbody>
</table>

D: Diopter
UCVA: Uncorrected visual acuity
BCVA: Best corrected visual acuity
Figure 1. Double angle polar plots showing the distribution of the surgically induced astigmatism between baseline and one month after surgery in the 2.8 mm (A) and 2.2 mm (B) group and between baseline and three months after surgery in the 2.8 mm (C) and 2.2 mm (D) group. The centroid of each circle shows the centroid of the surgically induced astigmatism in each group and the circle itself represents the standard deviation.
Figure 2. Double angle polar plots showing the distribution of the surgically induced astigmatism in inferotemporal incision (right eye) between baseline and one month after surgery in the 2.8 mm (A) and 2.2 mm (B) group and between baseline and three months after surgery in the 2.8 mm (C) and 2.2 mm (D) group.
Figure 3. Double angle polar plots showing the distribution of the surgically induced astigmatism in superotemporal incision (left eye) between baseline and one month after surgery in the 2.8 mm (A) and 2.2 mm (B) group and between baseline and three months after surgery in the 2.8 mm (C) and 2.2 mm (D) group.
Discussion

Surgically induced astigmatism

Advancements in the phacoemulsification technique and performing surgery through a smaller incision has resulted in less change in corneal parameters and less residual refractive error, and thus better refractive results after surgery, provided that IOL power is calculated precisely.

SIA can be calculated in different ways. In this study, SIA was calculated using the Holladay 10-step formula\(^5\) and to represent the axes of SIA, it was reported in a double angle polar plot.\(^6\)

Mean SIA in our study was <0.1 D in both groups at all follow-up visits, and clinically insignificant (P>0.05). Our results are consistent with those of Pfleger et al\(^7\) who reported SIA of 0.17 D after 6 months and 0.09 D after 1 year; however, their surgical approach included a temporal incision. In studies where oblique incisions are made, the amount of SIA has been reported to be 0.42 by Wilczynski et al\(^8\) 0.60 D by Ermis et al\(^9\), 0.68 D by Beltrame et al\(^10\) and 0.89 D by Rainer et al.\(^11\) Although we used oblique incisions, mean SIA was much lower than that in other studies. CCIs lead to flattening in the meridian of the incision and steepening in the meridian 90 degrees away. In our surgical method, we created only two incisions 90 degrees apart, and they might have had counter effects on each other. This could explain the small amount of SIA in our study one month and three months after surgery in both groups. To create the most flattening effect on a meridian, the wound must be perpendicular to the corneal surface. In our technique, we made a steep uniplanar wound with no perpendicular component that can also justify the small SIA in our study.

To compare SIA induced by different wound locations, we analyzed SIA in each group separately in 2.2 mm and 2.8 mm groups; however, the difference was not clinically significant as indicated previously in our results. Nielsen and coworkers\(^12\) stated that changing the position of CCI only changes the direction of SIA. Beltrame et al\(^10\) also found similar amounts of SIA in right and left eyes (superotemporal and superonasal), respectively. Borasio et al\(^3\) found significantly less SIA eight weeks after surgery in the group with a temporal CCI compared to the steep meridian, but the difference was not significant 3 months after surgery. Ermis et al\(^5\) found no difference in SIA when they compared superonasal and superotemporal incisions, but there were some differences in the horizontal component of the SIA. Kohnen and coauthors\(^13\) reported more SIA in nasal versus temporal scleral tunnel incisions, especially in the early postoperative period and suggested that it could be the result of the steeper wound of a nasal incision or the closer location of the nasal incision to the corneal center. Another possible cause of different amounts of SIA with different incision sites is the effect of the lids on the corneal morphology. However, our study subgroup analysis showed no clinically different SIA regarding incision site.

Effective phacoemulsification time

Although we found no significant inter-group difference in mean EPT values (P=0.2), they were slightly higher than the values reported by Alio et al\(^14\) (9.2±12.38 sec) for their coaxial group with 3.0 mm incisions, Mencucci et al\(^15\) (10±8 sec), and Cavallini et al\(^16\) (4.94±2.99 sec), probably because the nuclear density in the latter studies ranged between 2 and 4 on the LOCS III scale while we had patients with up to grade 6. EPT, as shown in our study, highly correlates with nucleus density (P<0.001) and this could explain the higher EPT in our study.

EPT can be calculated by multiplying the mean ultrasound power by the phacoemulsification time. In a study comparing microincision (2.2 mm) versus standard (2.8 mm) clear corneal cataract surgery, mean cumulative dissipated energy was 6.64±3.82 in the 2.8 mm incision group and 5.07±3.14 in the 2.2 mm group; the difference was significant but this could be attributed to the use of different phaco tip configurations in the two groups,\(^2\) as there was no inter-group difference in our study by using similar phaco tip configurations.

Endothelial cell loss

In our study, endothelial cell loss was 6.05±7.5% in the 2.8 mm group and 10.09±9.2% in the 2.2 mm group. Although ECC was higher in the 2.2 mm group 3 months after surgery, the difference was not
statistically significant (P=0.07). This result is consistent with equal EPT, duration of surgery and BSS volume used in the two groups.

In the general population, ECC decreases with age by 0.5-0.8% per year.\(^{17}\) Phacoemulsification leads to endothelial cell loss and the process may continue for at least 10 years after surgery\(^ {18}\) or even throughout a patient’s life. The causes of this cell loss are corneal distortion, irrigation solution turbulence, trauma induced by instrument manipulation, nuclear fragments floating in the AC during phacoemulsification, possible IOL contact, and free oxygen radicals. On the other hand, hyaluronic acid may have a protective effect due to its mechanical and chemical properties.\(^ {19}\) Wilczynski et al found 9.46% endothelial cell loss in a study using coaxial phacoemulsification through a 1.8 mm incision.\(^ {20}\) Berdahl et al\(^ {2}\) found more endothelial cell loss in their 2.8 mm incision versus 2.2 mm coaxial microincision cataract surgery (MICS) groups (P=0.044), but 30 and 40 degree bevel Kelman configurations were used for their 2.8 mm and 1.6 mm incisions, respectively. It has been demonstrated that differences in the tip configuration can influence various aspects of phacoemulsification and so lead to varying degrees of endothelial cell loss. The endothelial cell loss was 6.51% in a study by Mencucci et al\(^ {19}\) who used a standard phacoemulsification technique similar to ours. However, as stated previously, nucleus density on the LOCS III scale was higher in our study. In other studies, endothelial cell loss has been reported to be 4.66\%,\(^ {21}\) 11.65\%\(^ {2}\) to 14.5\%,\(^ {22}\) and it is suggested to correlate with the amount of fluid circulating in the AC. In a comparative study between conventional phacoemulsification and coaxial MICS using 2.8 mm and 1.6 mm incisions,\(^ {23}\) the difference in the endothelial cell loss was not significant and was independent of surgery time and ultrasound time that were significantly higher in the coaxial MICS group. The inconsistency of these observations has been attributed to less acoustic power generation when using smaller phaco tips. The size difference between two phaco tips used in our study was less than those used by Dosso et al. The surgeon skill, instrument handling practice, and preferred surgical technique can also influence the amount of endothelial cell loss.\(^ {24}\)

**Corneal thickness**

Mean CCT increased from 528±32 μm to 565±38 μm three days after surgery in the 2.8 mm group and from 535±36 μm to 567±45 μm in the 2.2 mm group; however, the difference between two groups was not statistically significant (P=0.35). Both groups returned to their baseline values one month after surgery; therefore, both groups were the same in terms of corneal edema. These results are consistent with those reported by Bardahl et al\(^ {20}\) and other investigators.\(^ {16,23,25}\) Woo et al\(^ {26}\) suggest SIA can be affected by changes in CCT; however, this was not the case in our study.

Another issue is IOL insertion though a smaller wound. We used Alcon SA60AT IOL since the feasibility of its implantation is already studied.\(^ {26,27}\) In our study, we used a wound assisted lens implantation technique that led to less wound enlargement.\(^ {28}\)

A cylindrical tube with a round cross-section is expected to cause more wound morphology change when inserted through a smaller incision than a larger incision, however, Berdahl et al demonstrated that wound architecture in their 2.2 mm incisions was superior to 2.75 mm ones, and both were superior to 1.2 mm incisions used in bimanual phacoemulsification.\(^ {1}\) The good wound architecture in both groups in our study was confirmed with no wound leakage in either group.

**Conclusion**

Although microincision coaxial phacoemulsification can be used by all surgeons who are familiar with conventional phacoemulsification and its safety and effectiveness, it showed minimum additional advantage in comparison with conventional phacoemulsification through a 2.8 mm incision specially regarding SIA which could be one of its most significant benefits.
References


