Macular function and morphology after peeling of idiopathic epiretinal membrane with and without the assistance of indocyanine green

J Hillenkamp, P Saikia, F Gora, H G Sachs, C P Lohmann, J Roider, W Bäumler, V-P Gabel

Aim: To investigate macular function and morphology after surgical removal of idiopathic epiretinal membrane (IEM) with and without assistance of indocyanine green (ICG).

Methods: A retrospective study as a consecutive case series, of 39 patients with IEM. 39 patients, 23 female, 16 male, mean age 67 years, underwent standard three port pars plana vitrectomy with removal of epiretinal membrane. Two groups of patients were consecutively operated: in 20 patients ICG 0.1% in glucose 5% was used to stain the epiretinal membrane. 19 patients underwent the identical procedure but without use of ICG. Postoperative follow up was 1–92 months (mean 15.5 months). Functional outcome was assessed with subjective improvement, best corrected visual acuity (BCVA), Amsler grid test, 10˚ and 30˚ automated perimetry (Heidelberg visual field analyser) (HFA), and Goldmann kinetic perimetry. Macular morphology was assessed with stereoscopic biomicroscopy and optical coherence tomography (OCT). The main outcome measures were macular function as determined by BCVA, presence of visual field defects, and metamorphopsia as determined by Amsler grid test, macular morphology as determined by slit lamp biomicroscopy, and OCT.

Results: BCVA improved in 28 patients, remained unchanged in eight patients, and decreased in three patients. Improvement of BCVA was statistically significant in both groups (p = 0.003). Mean BCVA in patients operated with ICG improved from 0.33 preoperatively to 0.53 postoperatively. Mean BCVA in patients operated without ICG improved from 0.32 preoperatively to 0.54 postoperatively. Reduction of macular oedema as measured by OCT was statistically significant in both groups (p<0.01). There was no statistically significant difference in postoperative BCVA, macular oedema as measured by OCT, postoperative Amsler grid test, and subjective improvement between the two groups. The incidence of residual or recurrent epiretinal membrane was greater in the group operated without ICG (p = 0.014).

Visual field defects were detected in one patient operated with ICG and in three patients operated without ICG. Postoperative Amsler grid test, and subjective improvement between the two groups. The incidence of residual or recurrent epiretinal membrane was greater in the group operated without ICG (p = 0.014).

Conclusions: Removal of epiretinal tissue with or without assistance of ICG improved visual function and reduced macular oedema in most patients. Adverse effects clearly attributable to the use of ICG were not observed but further investigation is warranted.

Idiopathic epiretinal membrane (IEM) is characterised by the formation of epimacular membrane system together with fibrocellular epiretinal membranes even when it was not intended.14 15 Several authors have reported good functional outcome of ICG assisted vitrectomy,12 16–18 whereas some authors have reported less favourable results in visual acuity,6 19 20 and significant visual field defects when intraocular ICG was used.6 19–21 Because of this controversy, a possible toxic effect of ICG on the inner retina has become the subject of an ongoing debate.

It was the aim of this study to retrospectively compare the functional and morphological outcome of epiretinal membrane peeling as a treatment for IEM with and without the assistance of ICG.

PATIENTS AND METHODS

The present study was designed as a retrospective analysis of two consecutive interventional case series. A total of 39 patients (23 female, 16 male) with a mean age of 67 years with IEM were retrospectively recruited. All patients

Abbreviations: BCVA, best corrected visual acuity; HFA, Heidelberg visual field analyser; ICG, indocyanine green; IEM, idiopathic epiretinal membrane; OCT, optical coherence tomography

See end of article for authors’ affiliations

Correspondence to: Dr Jost Hillenkamp, Eye Hospital, University of Regensburg, Franz-Josef-Strauss-Allee 11, D-93042 Regensburg, Germany. hillenka@hotmail.com

Accepted for publication 1 August 2004
complained preoperatively of reduced visual acuity and metamorphopsia. Twenty patients were operated with the aid of ICG and 19 patients underwent the same surgical procedure but without the aid of ICG. All patients of the group operated without ICG were operated before the introduction of ICG staining in macular surgery in our hospital during 2001. All patients were operated by experienced surgeons (HGS, CPL, JR, V-PG). Surgeons commenced applying ICG at different times during 2001. Patients with other retinal disease, glaucoma or postoperative retinal detachment were excluded from the study.

**Surgical technique**

All patients underwent standard three port pars plana vitrectomy, including where necessary the induction of a posterior vitreous detachment. Balanced salt solution (BSS; Alcon Laboratories, Fort Worth, TX, USA) was used as an irrigation solution. In the group operated without ICG the epiretinal membrane was engaged with intraocular forceps to create a flap and then peeled from the nerve fibre layer usually in a capsulorrhexis fashion before a routine closure without the use of tamponade agents. In the group operated with ICG the continuous BSS irrigation was briefly stopped and less than 0.5 ml of ICG (Pulsion Medical Systems AG, Munich, Germany) at a 0.1% concentration dissolved in glucose 5% was injected into the BSS filled globe just above the posterior pole. The osmolarity of this solution was 296 mOsm as measured with an osmometer (Knauer, Berlin, Germany). After less than 1 minute, the irrigation was restarted and thus the dye was quickly washed out of the globe. The epiretinal membrane was stained at a faint green colour and was clearly visible under illumination from the standard light pipe of the vitrectomy instrument. The stained membrane was engaged with intraocular forces and peeled in the same manner as in the patients operated without ICG before routine closure without the use of tamponade agents. Complete removal of all epiretinal membranous tissue was attempted in all patients in both groups. The delamination of epiretinal membranous tissue usually led to a complete removal of all visible epiretinal tissue and peeling of the underlying internal limiting membrane was only attempted in a capsulorrhexis fashion before a routine closure without the use of tamponade agents. Complete removal of all epiretinal membranous tissue was attempted in all patients in both groups. The delamination of epiretinal membranous tissue usually led to a complete removal of all visible epiretinal tissue and peeling of the underlying internal limiting membrane was only attempted in patients operated without ICG before routine closure without the use of tamponade agents. Complete removal of all epiretinal membranous tissue was attempted in all patients in both groups. The delamination of epiretinal membranous tissue usually led to a complete removal of all visible epiretinal tissue and peeling of the underlying internal limiting membrane was only attempted in patients operated without ICG before routine closure without the use of tamponade agents. Complete removal of all epiretinal membranous tissue was attempted in all patients in both groups. The delamination of epiretinal membranous tissue usually led to a complete removal of all visible epiretinal tissue and peeling of the underlying internal limiting membrane was only attempted in patients operated without ICG before routine closure without the use of tamponade agents. Complete removal of all epiretinal membranous tissue was attempted in all patients in both groups. The delamination of epiretinal membranous tissue usually led to a complete removal of all visible epiretinal tissue and peeling of the underlying internal limiting membrane was only attempted in patients operated without ICG before routine closure without the use of tamponade agents. Complete removal of all epiretinal membranous tissue was attempted in all patients in both groups.

**Measurement of the emission spectrum of the light source**

The spectral distribution of the light source emission was measured using an optical multichannel analyser (Spex 270M, Jobin Yvon, Munich, Germany). The emission of the light source was fed into the spectrograph (0.1 mm entrance slot) and detected by the cooled CCD camera in the spectral range of 590–908 nm with a resolution of 1 nm. The optical output of the light source was measured through the light fibre. The fibre of the light source was directly connected to the light fibre of the spectrograph to measure qualitatively the light distribution.

**RESULTS**

We investigated the outcome of surgical peeling of IEM in two groups of patients: patients operated with and without the aid of ICG.

The following parameters were not statistically significantly different between the two groups: 15 of 20 patients operated with ICG reported an overall subjective improvement of visual function since the operation versus 16 of 19 patients in the group operated without ICG (p = 0.73, χ² test, Fisher's test). Metamorphopsia had subjectively improved in 15 of 20 patients operated with ICG and in 13 of 19 patients operated without ICG (p = 0.73, χ² test, Fisher's test).

One patient in the group operated with ICG had a paracentral nasal visual field defect in the HFA and Goldmann perimetry (fig 1, patient 15). Three patients in the group operated without ICG had visual field defects: One lower temporal peripheral defect in the Goldmann perimetry (fig 2, patient 23), one paracentral nasal defect in the HFA and Goldmann perimetry (fig 3, patient 24), and one paracentral defect in the HFA 10⁶ perimetry (fig 4, patient 30). There were two additional patients with visual field defects in each group but these non-specific defects were recorded only by HFA with extensive losses of fixation suggesting an unreliable test result which was not reproducible by Goldmann perimetry (table 1). These defects were not taken into account in the data analysis. All visual field defects were asymptomatic.

The normalised emission spectrum of the light source and the normalised absorption spectra of ICG dissolved in water or in 5% glucose showed an overlap (fig 5).

**DISCUSSION**

Our results show no statistically significant difference in macular function as assessed by preoperative and postoperative BCVA, Amsler grid test, or subjective improvement of overall visual function and metamorphopsia between the groups operated with and without the aid of ICG. BCVA improved in both groups. In accordance with the findings of others' macular oedema improved with surgery. The reduction of macular oedema as assessed by OCT measurement of foveal retinal thickness was not statistically significantly different between the two groups. The incidence of residual or recurrent epiretinal membrane was greater in the group operated without ICG. This finding may be related to the longer follow up period which could be a reason for a greater number of recurrent membrane formation in that group. Alternatively, this finding may be related to a greater number of incomplete removals of epiretinal membrane possibly because not all membranous tissue could be intraoperatively visualised without the aid of ICG staining. A distinction between these two possible causes must be made by a future suitably designed prospective randomised trial. Furthermore, the present study has some of the usual limitations of retrospective analyses. We cannot exclude the presence of the
<table>
<thead>
<tr>
<th>Patient No</th>
<th>Group</th>
<th>Sex</th>
<th>Age (years)</th>
<th>Eye</th>
<th>Surgeon</th>
<th>Follow up (months)</th>
<th>Subjective improvement</th>
<th>Subjective improvement of metamorphopsia</th>
<th>Amsler VA preop</th>
<th>VA postop</th>
<th>Defect in HFA postop</th>
<th>Defect in Goldmann postop</th>
<th>OCT preop (μm)</th>
<th>OCT postop (μm)</th>
<th>Lens preop</th>
<th>Lens postop</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>ICG</td>
<td>F</td>
<td>65</td>
<td>RE</td>
<td>HGS</td>
<td>5</td>
<td>Yes</td>
<td>Yes</td>
<td>Positive</td>
<td>0.3</td>
<td>0.5</td>
<td>–</td>
<td>–</td>
<td>No</td>
<td>545</td>
<td>233</td>
</tr>
<tr>
<td>2</td>
<td>ICG</td>
<td>F</td>
<td>57</td>
<td>RE</td>
<td>HGS</td>
<td>4</td>
<td>Yes</td>
<td>Yes</td>
<td>Negative</td>
<td>0.2</td>
<td>0.3</td>
<td>–</td>
<td>–</td>
<td>No</td>
<td>486</td>
<td>258</td>
</tr>
<tr>
<td>3</td>
<td>ICG</td>
<td>M</td>
<td>62</td>
<td>RE</td>
<td>HGS</td>
<td>5</td>
<td>No</td>
<td>Yes</td>
<td>Positive</td>
<td>0.4</td>
<td>0.4</td>
<td>–</td>
<td>–</td>
<td>No</td>
<td>303</td>
<td>250</td>
</tr>
<tr>
<td>4</td>
<td>ICG</td>
<td>M</td>
<td>56</td>
<td>LE</td>
<td>VPG</td>
<td>9</td>
<td>Yes</td>
<td>No</td>
<td>Positive</td>
<td>0.5</td>
<td>0.6</td>
<td>–</td>
<td>–</td>
<td>No</td>
<td>352</td>
<td>317</td>
</tr>
<tr>
<td>5</td>
<td>ICG</td>
<td>F</td>
<td>66</td>
<td>RE</td>
<td>CPL</td>
<td>8</td>
<td>No</td>
<td>No</td>
<td>Positive</td>
<td>0.2</td>
<td>0.2</td>
<td>–</td>
<td>–</td>
<td>No</td>
<td>516</td>
<td>351</td>
</tr>
<tr>
<td>6</td>
<td>ICG</td>
<td>F</td>
<td>55</td>
<td>RE</td>
<td>VPG</td>
<td>4</td>
<td>Yes</td>
<td>Yes</td>
<td>Negative</td>
<td>0.5</td>
<td>0.5</td>
<td>–</td>
<td>–</td>
<td>No</td>
<td>310</td>
<td>334</td>
</tr>
<tr>
<td>7</td>
<td>ICG</td>
<td>M</td>
<td>77</td>
<td>RE</td>
<td>JR</td>
<td>24</td>
<td>No</td>
<td>No</td>
<td>Positive</td>
<td>0.5</td>
<td>0.3</td>
<td>–</td>
<td>–</td>
<td>No</td>
<td>510</td>
<td>291</td>
</tr>
<tr>
<td>8</td>
<td>ICG</td>
<td>M</td>
<td>66</td>
<td>RE</td>
<td>VPG</td>
<td>1</td>
<td>Yes</td>
<td>Yes</td>
<td>Positive</td>
<td>0.25</td>
<td>0.5</td>
<td>Defect</td>
<td>–</td>
<td>No</td>
<td>333</td>
<td>333</td>
</tr>
<tr>
<td>9</td>
<td>ICG</td>
<td>F</td>
<td>73</td>
<td>RE</td>
<td>CPL</td>
<td>5</td>
<td>Yes</td>
<td>Yes</td>
<td>Negative</td>
<td>0.3</td>
<td>0.3</td>
<td>–</td>
<td>–</td>
<td>Yes</td>
<td>311</td>
<td>250</td>
</tr>
<tr>
<td>10</td>
<td>ICG</td>
<td>M</td>
<td>72</td>
<td>LE</td>
<td>VPG</td>
<td>9</td>
<td>Yes</td>
<td>No</td>
<td>Positive</td>
<td>0.5</td>
<td>0.5</td>
<td>–</td>
<td>–</td>
<td>No</td>
<td>633</td>
<td>492</td>
</tr>
<tr>
<td>11</td>
<td>ICG</td>
<td>F</td>
<td>70</td>
<td>LE</td>
<td>CPL</td>
<td>12</td>
<td>Yes</td>
<td>Yes</td>
<td>Positive</td>
<td>0.4</td>
<td>1</td>
<td>–</td>
<td>–</td>
<td>No</td>
<td>415</td>
<td>258</td>
</tr>
<tr>
<td>12</td>
<td>ICG</td>
<td>F</td>
<td>73</td>
<td>RE</td>
<td>VPG</td>
<td>5</td>
<td>Yes</td>
<td>Yes</td>
<td>Positive</td>
<td>0.5</td>
<td>1</td>
<td>–</td>
<td>–</td>
<td>No</td>
<td>628</td>
<td>291</td>
</tr>
<tr>
<td>13</td>
<td>ICG</td>
<td>F</td>
<td>62</td>
<td>RE</td>
<td>VPG</td>
<td>9</td>
<td>Yes</td>
<td>Yes</td>
<td>Negative</td>
<td>0.16</td>
<td>1.2</td>
<td>–</td>
<td>–</td>
<td>No</td>
<td>233</td>
<td>283</td>
</tr>
<tr>
<td>14</td>
<td>ICG</td>
<td>F</td>
<td>59</td>
<td>RE</td>
<td>VPG</td>
<td>27</td>
<td>Yes</td>
<td>Yes</td>
<td>Positive</td>
<td>0.3</td>
<td>0.7</td>
<td>–</td>
<td>–</td>
<td>No</td>
<td>158</td>
<td>158</td>
</tr>
<tr>
<td>15</td>
<td>ICG</td>
<td>F</td>
<td>65</td>
<td>LE</td>
<td>VPG</td>
<td>11</td>
<td>Yes</td>
<td>Yes</td>
<td>Positive</td>
<td>0.2</td>
<td>0.6</td>
<td>Defect</td>
<td>Defect</td>
<td>No</td>
<td>497</td>
<td>332</td>
</tr>
<tr>
<td>16</td>
<td>ICG</td>
<td>M</td>
<td>52</td>
<td>LE</td>
<td>VPG</td>
<td>7</td>
<td>No</td>
<td>No</td>
<td>Positive</td>
<td>0.8</td>
<td>0.7</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>17</td>
<td>ICG</td>
<td>F</td>
<td>66</td>
<td>RE</td>
<td>HGS</td>
<td>22</td>
<td>Yes</td>
<td>Yes</td>
<td>Positive</td>
<td>0.3</td>
<td>0.7</td>
<td>–</td>
<td>–</td>
<td>No</td>
<td>158</td>
<td>183</td>
</tr>
<tr>
<td>18</td>
<td>ICG</td>
<td>M</td>
<td>59</td>
<td>LE</td>
<td>HGS</td>
<td>3</td>
<td>Yes</td>
<td>Yes</td>
<td>Positive</td>
<td>0.16</td>
<td>0.4</td>
<td>Defect</td>
<td>–</td>
<td>No</td>
<td>549</td>
<td>358</td>
</tr>
<tr>
<td>19</td>
<td>ICG</td>
<td>M</td>
<td>71</td>
<td>LE</td>
<td>HGS</td>
<td>8</td>
<td>No</td>
<td>Yes</td>
<td>Positive</td>
<td>0.4</td>
<td>0.6</td>
<td>–</td>
<td>–</td>
<td>No</td>
<td>367</td>
<td>250</td>
</tr>
<tr>
<td>20</td>
<td>ICG</td>
<td>M</td>
<td>70</td>
<td>RE</td>
<td>HGS</td>
<td>10</td>
<td>Yes</td>
<td>Yes</td>
<td>Positive</td>
<td>0.5</td>
<td>0.6</td>
<td>–</td>
<td>–</td>
<td>Yes</td>
<td>462</td>
<td>242</td>
</tr>
<tr>
<td>21</td>
<td>No ICG</td>
<td>F</td>
<td>67</td>
<td>RE</td>
<td>HGS</td>
<td>7</td>
<td>Yes</td>
<td>No</td>
<td>Positive</td>
<td>0.4</td>
<td>0.3</td>
<td>–</td>
<td>–</td>
<td>Yes</td>
<td>544</td>
<td>558</td>
</tr>
<tr>
<td>22</td>
<td>No ICG</td>
<td>F</td>
<td>62</td>
<td>LE</td>
<td>VPG</td>
<td>12</td>
<td>No</td>
<td>No</td>
<td>Positive</td>
<td>0.5</td>
<td>0.5</td>
<td>–</td>
<td>–</td>
<td>No</td>
<td>359</td>
<td>275</td>
</tr>
<tr>
<td>23</td>
<td>No ICG</td>
<td>F</td>
<td>67</td>
<td>RE</td>
<td>HGS</td>
<td>6</td>
<td>Yes</td>
<td>Yes</td>
<td>Positive</td>
<td>0.2</td>
<td>0.3</td>
<td>–</td>
<td>Defect</td>
<td>Yes</td>
<td>225</td>
<td>225</td>
</tr>
<tr>
<td>24</td>
<td>No ICG</td>
<td>F</td>
<td>32</td>
<td>RE</td>
<td>VPG</td>
<td>7</td>
<td>No</td>
<td>No</td>
<td>Negative</td>
<td>0.4</td>
<td>0.4</td>
<td>Defect</td>
<td>Defect</td>
<td>Yes</td>
<td>311</td>
<td>363</td>
</tr>
<tr>
<td>25</td>
<td>No ICG</td>
<td>F</td>
<td>68</td>
<td>LE</td>
<td>VPG</td>
<td>10</td>
<td>Yes</td>
<td>Yes</td>
<td>Positive</td>
<td>0.3</td>
<td>0.6</td>
<td>Defect</td>
<td>–</td>
<td>No</td>
<td>517</td>
<td>284</td>
</tr>
<tr>
<td>26</td>
<td>No ICG</td>
<td>M</td>
<td>72</td>
<td>LE</td>
<td>VPG</td>
<td>7</td>
<td>Yes</td>
<td>Yes</td>
<td>Positive</td>
<td>0.3</td>
<td>0.5</td>
<td>–</td>
<td>–</td>
<td>No</td>
<td>508</td>
<td>317</td>
</tr>
<tr>
<td>27</td>
<td>No ICG</td>
<td>F</td>
<td>74</td>
<td>RE</td>
<td>VPG</td>
<td>8</td>
<td>Yes</td>
<td>Yes</td>
<td>Positive</td>
<td>0.6</td>
<td>0.9</td>
<td>–</td>
<td>–</td>
<td>No</td>
<td>268</td>
<td>216</td>
</tr>
<tr>
<td>28</td>
<td>No ICG</td>
<td>M</td>
<td>76</td>
<td>RE</td>
<td>VPG</td>
<td>12</td>
<td>Yes</td>
<td>Yes</td>
<td>Positive</td>
<td>0.4</td>
<td>0.6</td>
<td>–</td>
<td>–</td>
<td>Yes</td>
<td>333</td>
<td>333</td>
</tr>
<tr>
<td>29</td>
<td>No ICG</td>
<td>M</td>
<td>76</td>
<td>RE</td>
<td>VPG</td>
<td>6</td>
<td>Yes</td>
<td>Yes</td>
<td>Negative</td>
<td>0.4</td>
<td>0.5</td>
<td>–</td>
<td>–</td>
<td>No</td>
<td>508</td>
<td>317</td>
</tr>
<tr>
<td>30</td>
<td>No ICG</td>
<td>M</td>
<td>75</td>
<td>RE</td>
<td>VPG</td>
<td>7</td>
<td>Yes</td>
<td>No</td>
<td>Positive</td>
<td>0.2</td>
<td>0.6</td>
<td>Defect</td>
<td>–</td>
<td>No</td>
<td>525</td>
<td>300</td>
</tr>
<tr>
<td>31</td>
<td>No ICG</td>
<td>M</td>
<td>72</td>
<td>RE</td>
<td>VPG</td>
<td>23</td>
<td>Yes</td>
<td>No</td>
<td>Positive</td>
<td>0.4</td>
<td>1</td>
<td>–</td>
<td>–</td>
<td>No</td>
<td>310</td>
<td>308</td>
</tr>
<tr>
<td>32</td>
<td>No ICG</td>
<td>F</td>
<td>78</td>
<td>RE</td>
<td>CPL</td>
<td>33</td>
<td>Yes</td>
<td>Yes</td>
<td>Negative</td>
<td>0.3</td>
<td>0.6</td>
<td>–</td>
<td>–</td>
<td>No</td>
<td>308</td>
<td>308</td>
</tr>
<tr>
<td>33</td>
<td>No ICG</td>
<td>M</td>
<td>61</td>
<td>LE</td>
<td>VPG</td>
<td>12</td>
<td>Yes</td>
<td>Yes</td>
<td>Negative</td>
<td>0.3</td>
<td>0.5</td>
<td>–</td>
<td>–</td>
<td>No</td>
<td>458</td>
<td>380</td>
</tr>
<tr>
<td>34</td>
<td>No ICG</td>
<td>M</td>
<td>87</td>
<td>LE</td>
<td>HGS</td>
<td>54</td>
<td>No</td>
<td>Yes</td>
<td>Positive</td>
<td>0.3</td>
<td>0.3</td>
<td>–</td>
<td>–</td>
<td>Yes</td>
<td>583</td>
<td>417</td>
</tr>
<tr>
<td>35</td>
<td>No ICG</td>
<td>F</td>
<td>63</td>
<td>RE</td>
<td>JR</td>
<td>46</td>
<td>Yes</td>
<td>Yes</td>
<td>Negative</td>
<td>0.3</td>
<td>0.1</td>
<td>–</td>
<td>–</td>
<td>No</td>
<td>273</td>
<td>273</td>
</tr>
<tr>
<td>36</td>
<td>No ICG</td>
<td>F</td>
<td>65</td>
<td>RE</td>
<td>VPG</td>
<td>11</td>
<td>Yes</td>
<td>Yes</td>
<td>Negative</td>
<td>0.4</td>
<td>1</td>
<td>–</td>
<td>–</td>
<td>Yes</td>
<td>308</td>
<td>308</td>
</tr>
<tr>
<td>37</td>
<td>No ICG</td>
<td>M</td>
<td>79</td>
<td>LE</td>
<td>VPG</td>
<td>92</td>
<td>Yes</td>
<td>Yes</td>
<td>Positive</td>
<td>0.4</td>
<td>0.5</td>
<td>Defect</td>
<td>–</td>
<td>Yes</td>
<td>350</td>
<td>350</td>
</tr>
<tr>
<td>38</td>
<td>No ICG</td>
<td>F</td>
<td>73</td>
<td>RE</td>
<td>HGS</td>
<td>9</td>
<td>Yes</td>
<td>Yes</td>
<td>Positive</td>
<td>0.4</td>
<td>0.3</td>
<td>–</td>
<td>–</td>
<td>No</td>
<td>458</td>
<td>426</td>
</tr>
<tr>
<td>39</td>
<td>No ICG</td>
<td>M</td>
<td>75</td>
<td>LE</td>
<td>VPG</td>
<td>24</td>
<td>Yes</td>
<td>Yes</td>
<td>Positive</td>
<td>0.4</td>
<td>0.6</td>
<td>–</td>
<td>–</td>
<td>No</td>
<td>414</td>
<td>325</td>
</tr>
</tbody>
</table>

*OCT determined macular retinal thickness of normal human eyes: 163.6 μm (foveal), 275.5 μm (parafoveal).*

*Commentaries to visual field: patients 8, 10, 11, 17–19, 25, 34, 37: loss of fixation.*
observed visual field defects before surgery. The relatively large number of surgeons and the fact that examiners were not blinded are possible sources of confounding. We cannot exclude that comparing non-contemporary groups of patients is a source of confounding as the surgeons may have had improved their skills when operating the second group of patients. The patients operated with ICG were younger than the patients operated without ICG. However, since all patients except one 32 year old patient were in the age group above 50 years the difference of patient ages is unlikely to have had a significant impact on the investigated outcome measures.

Our findings in postoperative visual acuity are in accordance with other authors who described a positive functional outcome of ICG assisted vitreous surgery. Our findings are in contrast with authors who described less favourable postoperative visual acuity and visual field defects after ICG assisted vitreous surgery. These reports have contributed to the concern that ICG as used in macular surgery may be toxic to the inner retina.

The histological examination of peeled membranes showed cellular elements leading to the hypothesis of ICG causing retinal damage by an alteration of the vitreoretinal interface, whereas another histological study revealed similar cellular elements on membranes that were peeled without the aid of ICG. A possible photosensitising effect after intraoperative illumination of the stained retina with light of wavelengths between 380 and 760 nm as emitted by commonly used vitrectomy light pipes leading to...
morphological damage of the inner retina has been reported.\textsuperscript{23,24} This finding was not confirmed by other investigations.\textsuperscript{25,26} A possible cytotoxic effect of ICG has been investigated in experimental studies. Enaida \textit{et al.} found direct dose dependent functional and morphological damage of the retina after intravitreous application of ICG in an in vivo rat model.\textsuperscript{27} The doses used in this study were within or below the range (0.05–5.0 mg/eye) of clinical application but in contrast with clinical practice, where the ICG solution is removed within seconds up to 1 minute, the authors left the ICG in the eye for 10 days before examination of the exposed retinas.\textsuperscript{27} The clinical relevance of the results is therefore questionable.

We found visual field defects in three patients operated without ICG versus one patient operated with ICG. It is a limitation of the present retrospective analysis that we cannot exclude the presence of the described asymptomatic visual field defects before surgery. However, the results do not show a correlation between the incidence of visual field defects and the use of ICG. Visual field defect after vitrectomy is a well known postoperative complication which has been attributed to a dehydration injury of the retina during fluid-air exchange.\textsuperscript{28–30} This mechanism is unlikely to have had a role in our patients since we did not perform a fluid-air exchange during surgery. Visual field defect after vitrectomy has also been attributed to traction during cortical vitreous peeling,\textsuperscript{31} to intraoperative fluctuations of intraocular pressure, to optic nerve damage from retrobulbar injection, or to direct intraoperative mechanical trauma to the optic nerve.\textsuperscript{32} Kim \textit{et al.} reported a visual field defect after uneventful surgical removal of epiretinal membrane. Electron microscopy of the removed membrane showed adhesion between the epiretinal membrane and axons of the nerve fibre layer in an area of internal limiting lamina defect.\textsuperscript{33}

We cannot conclude from our data which mechanism caused the visual defects in our patients but our data do not support the hypothesis of ICG as a likely cause. As cited above, there is principal experimental evidence of a direct dose dependent cytotoxic effect of ICG.\textsuperscript{27} Also, phototoxicity of ICG irradiated with a diode laser emitting light at a wavelength of 805 nm has been studied in vitro. As the result, the photodynamic effect of ICG was related to the amount of ICG and the energy density of the illumination.\textsuperscript{34,35} The comparison of the emission spectrum of the light source used in the present study and the absorption spectrum of ICG show an overlap (Fig 5) and a phototoxic effect can therefore not be excluded. However, the studies mentioned do not necessarily reflect the actual intraoperative situation in macular surgery.

**Table 2**

<table>
<thead>
<tr>
<th>Patient group</th>
<th>Age (years)</th>
<th>Follow up (months)</th>
<th>BCVA preop (logMAR)</th>
<th>BCVA postop (logMAR)</th>
<th>Improvement of BCVA with surgery (logMAR)</th>
<th>Amsler grid test (positive postop)</th>
<th>Macular retinal thickness preop (micron OCT)</th>
<th>Macular retinal thickness postop (micron OCT)</th>
<th>Reduction of macular retinal thickness (micron OCT) with surgery</th>
<th>Macular epiretinal membrane postop (number of patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td>With ICG (n=20)</td>
<td>64.8 (6.9)</td>
<td>9.5 (7.1)</td>
<td>0.48 (0.21)</td>
<td>0.28 (0.2)</td>
<td>0.20 (0.1)</td>
<td>16 of 20</td>
<td>472 (143)</td>
<td>415 (114)</td>
<td>57 (11)</td>
<td>16 of 20</td>
</tr>
<tr>
<td>Without ICG (n=19)</td>
<td>69.6 (11.2)</td>
<td>20.3 (11.2)</td>
<td>0.49 (0.18)</td>
<td>0.27 (0.18)</td>
<td>0.22 (0.19)</td>
<td>12 of 19</td>
<td>415 (114)</td>
<td>347 (85)</td>
<td>84 (94)</td>
<td>12 of 19</td>
</tr>
</tbody>
</table>

All values given as mean (SD).

**Figure 5** The normalised emission spectrum (solid line) of the light source (Xenophot 6463HFXEFR, 15V, 150W, Osram, Germany) and the normalised absorption spectrum of ICG in water (dotted line) and in glucose 5% (broken line).
The absorption spectrum of ICG was very similar when dissolved in water or glucose 5% (fig 5). This is in contrast with Haritoglou et al who compared glucose 5% and balanced salt solution as solvents using lower concentrations of ICG than those used in the present study. They reported a variation in absorption depending on the solvent medium, with a shift towards higher wavelengths when glucose 5% was used as a solvent compared to balanced salt solution.19

In principle, retinal toxicity of ICG in macular surgery can be expected to depend on the concentration of the ICG solution, the osmolarity of the solution,17 the length of time before ICG is removed from the eye,18 whether ICG is injected into an air filled or a fluid filled eye (with less toxicity in fluid filled eyes),19 and the emission spectrum and the energy density of the illumination (fig 5).20 21 However, the question of a specific toxicity threshold of the retina for ICG remains unanswered. Our results suggest that ICG assisted macular surgery for IEM in the setting described in the present study did not cause retinal toxicity detectable with the diagnostic tests applied. Less favourable results in visual acuity and visual field defects in some other studies may have been caused by a higher ICG concentration20 21 and/or hypo-osmolarity of the solvent.19 20 21 26 A recent experimental study showed retinal toxicity after subretinal but not after epiretinal application of ICG in rabbits.29 Therefore, retinal toxicity may also depend on the type of macular surgery, possibly because the full thickness retinal hole allows direct contact of ICG with deeper retinal layers and the RPE in macular hole surgery20 28 but not in IEM surgery.

In summary, the results of the present study add relevant clinical data to the current controversial debate on the safety of ICG. ICG and other dyes should be used cautiously. Since ICG staining did not lead to better functional results in the present study and adverse effects can not yet be fully excluded, we recommend its use in epiretinal membrane peeling only when the membrane can otherwise not be safely removed. The functional and morphological results of the present study suggest that removal of epiretinal tissue with or without assistance of ICG improves visual function and reduces macular oedema in most patients.

The influence of enhanced cataract formation following vitrectomy must be taken into consideration in the evaluation of the functional outcome of our patients. Most of our patients whose visual acuity did not significantly improve were operated with surgical membrane peeling alone. Therefore, it seems reasonable to recommend concomitant lens surgery in all patients older than 60 years.

ACKNOWLEDGEMENT
Indocyanine green was a kind gift from Pulsion Medical Systems AG, Munich, Germany.

Authors’ affiliations
J Hillenkamp, P Saikia, F Gora, H G Sachs, C P Lohmann, V-P Gabel, Department of Ophthalmology, University of Regensburg, Germany
J Roider, Department of Ophthalmology, Universitätsklinikum Schleswig-Holstein, Campus Kiel, Kiel, Germany
W Bümmler, Department of Dermatology, University of Regensburg, Germany

Competing interests: None of the authors has a financial interest in indocyanine green.

Ethical approval: Approval was obtained from the ethics committee of the University of Regensburg.

REFERENCES
Macular function and morphology of idiopathic epiretinal membrane


www.bjophthalmol.com
Macular function and morphology after peeling of idiopathic epiretinal membrane with and without the assistance of indocyanine green

J Hillenkamp, P Saikia, F Gora, H G Sachs, C P Lohmann, J Roider, W Bäumler and V-P Gabel

doi: 10.1136/bjo.2004.051250

Updated information and services can be found at:
http://bjo.bmj.com/content/89/4/437

These include:

References
This article cites 37 articles, 7 of which you can access for free at:
http://bjo.bmj.com/content/89/4/437#BIBL

Email alerting service
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Topic Collections
Articles on similar topics can be found in the following collections

Retina (1608)
Ophthalmologic surgical procedures (1223)

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/