Artigo Original

# Internal limiting membrane inverted flap technique: a new paradigm in large macular hole surgery

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## RESUMO

**Objetivo:** Avaliar e eficácia e a segurança da pelagem da membrana limitante interna (MLI) com a técnica dos flaps invertidos (TFI) na cirurgia do buraco macular (BM) grande.
**Material e Métodos:** Análise retrospetiva dos pacientes com BMs grandes submetidos a vitrectomia com pelagem da MLI com a TFI entre Janeiro de 2013 e Dezembro de 2014, com um seguimento mínimo de 6 meses. Compararam-se os valores de MAVC pré e pós-operatórios e avaliou-se o encerramento documentado por OCT e a ocorrência de complicações. O teste de Wilcoxon foi usado para comparar a melhor acuidade visual corrigida, MAVC ($p<0,05$).
**Resultados:** Estudaram-se 17 olhos de 17 pacientes. 76,5% tinham BMs primários, 11,8% pós-vitrectomia e 11,8% traumáticos. O diâmetro mínimo médio foi de 578,5 ± 147μm e a duração média da sintomatologia foi de 35,9 meses. 47,1% dos olhos eram fáquicos, 11,8% tinham catarata e 41,2% eram pseudofáquicos. A cirurgia de catarata concomitante foi realizada em 47,1% dos casos. Para o seguimento médio de 7,76 meses a taxa de encerramento foi de 100%. A MAVC melhorou de 1,20 ± 0,48 para 0,68 ± 0,36 unidades logMar. A MAVC melhorou em todos os olhos, com 64,7% a ganhar duas ou mais linhas de Snellen. A taxa de complicações foi de 5,6%.
**Conclusões:** A pelagem da MLI com a TFI é eficaz e segura. Neste estudo, com BMs grandes, o sucesso anatómico foi 100% e a MAVC melhorou de forma estatisticamente significativa.

**Palavras-chave**
Membrana limitante interna, técnica dos flaps invertidos, buraco macular, cirurgia.

## ABSTRACT

**Purpose:** To evaluate the efficacy and safety of the internal limiting membrane (ILM) inverted flap technique (IFT) in large macular hole (MH) surgery.
**Material and Methods:** Retrospective analysis of eyes of patients with large MHs who underwent vitrectomy with ILM IFT between January 2013 and December 2014, with a minimum follow-up of 6 months. Myopic macular holes were excluded. We evaluated best-corrected visual acuity (BCVA), hole closure documented by OCT and complications.
We compared preoperative and postoperative values.

The Wilcoxon test was used for comparing BCVA ($p < 0.05$).
**Results:** 17 eyes of 17 patients with a mean age of 63.24 years were studied. 76.5% of eyes had primary MHs, 11,8% post-vitrectomy and 11,8% post-traumatic. Mean minimum MH diameter was 578,5 ± 147μm and the mean MH duration was 35,9 months. According to lens status, 47,1% were phakic, 11,8% had cataract and 41,2% were pseudophakic. Concomitant cataract surgery was performed in 47,1% of cases.
At the mean follow-up of 7,76 months, closure rate was 100%, with BCVA improving from 1,20 ± 0,48 to 0,68 ± 0,36 logMar units. All patients improved BCVA, with 64,7% gaining two or more Snellen lines of BCVA. Complication rate was 5.6%.
**Conclusions:** ILM IFT is an effective and safe technique in MH surgery. In this study, with large MH, the anatomic success rate was 100% and BCVA improvement was significant.

**Key-words**
Internal limiting membrane, inverted flap technique, macular hole surgery.

## INTRODUCTION

Macular hole (MH) was until twenty-five years ago an incurable disease and a main cause of legal blindness. And so it was until Kelly and Wendel[12] in 1991 proposed pars plana vitrectomy with posterior hyaloid peeling and air--fluid exchange to treat MH. With this approach, the main source of anterior-posterior traction on the retina was eliminated and the borders of the MH were dehydrated and approximated to facilitate glial proliferation and cellular migration. The first results claimed a closure rate of 58%[1].

In 1997, Eckhart et al.[5], in the light of knowledge of the importance of tangential traction exerted by the contraction of myofibroblasts over the internal limiting membrane (ILM) in the aetiology of MH[8], introduced the ILM peeling as part of MH surgery. ILM peeling relieves tangential traction, but also seems to stimulate glial cells to proliferate, increases retina elasticity and ensures the complete removal of an epiretinal membrane[22]. This meticulous procedure was later aided, in 2000, with the introduction of indocianine green by Brooks et al.[3] to stain the ILM, which made the peeling safer and more effective. Independently of the questions related to indocianine green retinal toxicity or the use of other more recent vital dyes such as infracianine blue, trypan blue, brilliant blue or lutein-based dyes, staining is mandatory[6] and closure rates around 90% can be found in most of the case-series published in the literature[1, 2, 6, 20].

Although conventional ILM peeling has an undeniable anatomical effect in relation to closure rate, its functional advantages are controversial and a recent systematic review found no differences in best-corrected visual acuity (BCVA)[20].

Apart from this issue, it is consensual that not all MHs close with conventional ILM peeling and that anatomic success is dependent on MH size, chronicity, pre-operative BCVA and aetiology[6, 18, 19, 21]. Particularly large MHs with a minimum diameter of 400μm, MHs with more than 1 year duration and all secondary MHs in general are associated with both a worse anatomic and functional outcome[19]. Moreover, in these cases, a "flat--open" outcome was considered a success, despite being associated with a poor visual outcome[19].

In 2010 Michalewska et al. presented the ILM inverted flap technique (IFT) for the treatment of large MHs[15]. It consists of an incomplete ILM peeling till the boundaries of the MH with inversion of its borders upside-down into the MH. The first results claimed a closure rate of 100% (when a free-flap did not occur), no "flat-open" appearance and a significant improvement in VA in relation to the conventional peeling[15].

In this article we proposed to evaluate the efficacy and safety of the ILM IFT in the management of large MH. To do it, we evaluated MH closure rate documented by spectral domain optical coherence tomography (SD--OCT), BCVA and complications.

## MATERIAL E METHODS

A longitudinal, retrospective, descriptive and observational study was performed.

We analysed the medical records of patients with large MHs undergoing surgery with the ILM IFT between January 2013 and December 2014. Only eyes with a minimum follow-up of 6 months were included.

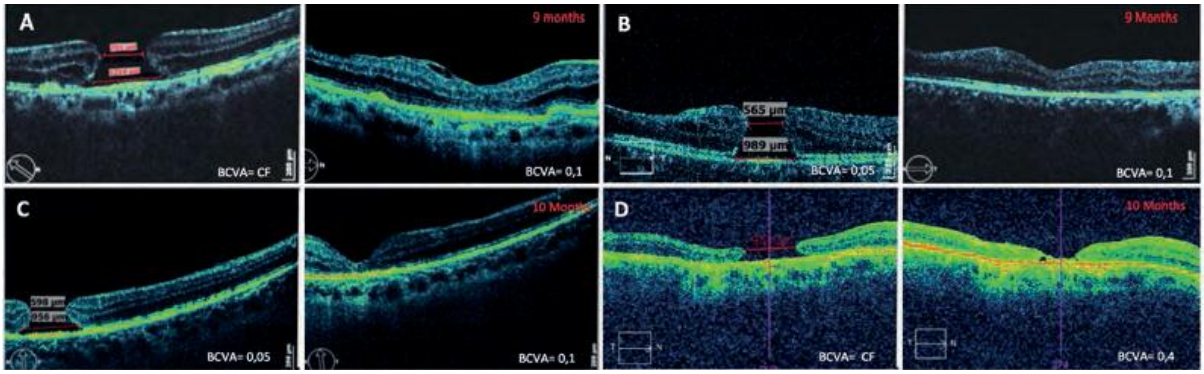


**Fig. 1 | SD-OCT scans (A,B and C – Copernicus, Optopol; D- Cirrus, Carl Zeiss) showing the preoperative (at left) and the post--operative (at right) images of some of the MH submitted to the ILM inverted flap technique.** Four examples are shown (A-D). All cases were primary MH, which duration was, respectively, 48 and 72 months in examples A and B and unknown in examples C and D. MH dimensions are shown with the calliper function of the OCT device (minimum diameters were, respectively, 701, 565, 568 and 963µm), BCVA is shown in the right-inferior corner of the image in Snellen decimal scale and the postoperative period is shown in the top-superior corner of the postoperative image.

We defined large MHs according to the new classification of the International Vitreomacular Traction Classification System[4], namely a full-thickness MH with a minimum diameter of 400 µm. Minimum diameter was calculated with the calliper function of our SD-OCT devices and was defined as the shortest distance, parallel to the retinal pigment epithelium, between the borders of the MH (Fig.1). We used Corpernicus SD-OCT (OPTOPOL Technology SA, Poland) or Cirrus SD-OCT (Carl Zeiss, Meditec, Dublin, CA).

We collected, in addition to the demographic data (age and sex), eye laterality and the post-operative follow-up, closure rate evaluated by SD-OCT, BCVA and complications. MH closure was defined as the absence of neurosensory defect over the fovea[11]. We compared the preoperative and postoperative values, for the average time of follow-up. For the study purposes, in order to homogenize the postoperative results, the last postoperative consultation between 6 and 12 months after surgery was considered.

All surgeries were performed by a single surgeon (RC). All patients underwent a 23G three –port pars plana vitrectomy, as a single procedure or combined with cataract surgery. Posterior hyaloid detachment was aided by triamcinolone acetonide and the vitreous base was vitrectomized with identation. Membrane blue-dual (tripan-blue 0,15% + brilliant blue 0,025%) was used to stain an eventual epiretinal membrane and the ILM. If an epiretinal membrane was present, it was peeled. An incomplete ILM peeling was performed, in a circular fashion, from a distance of at least 2 disc diameters until the MH edges where the ILM was left attached. After cutting the peripheral edges of the ILM with the vitrectome with low aspiration until a one and a half hole diameter size, its central remnants hanging in the vitreous cavity were inverted over the hole. The peeling was then enlarged up to the vascular arcades. After a low--pressure fluid-air exchange (around 15-20mmHg), the air was replaced with 20% SF6. The patient was kept in face--down position for 3 days.

Statistical analysis was performed using the software IBM Statistical Package for Social Sciences (SPSS) version 20.0®. BCVA was evaluated in Snellen charts and converted into the logarithm of the minimal angle of resolution (logMar) for statistical analysis. "Counting fingers" (CF) visual acuity was globally considered as 0,01 in decimal Snellen scale and later converted into logMar units. The normality of the variables was checked using the Kolmogorov-Smirnov test. Due to absence of normality, the Wilcoxon test was used to compare BCVA. A p value <0,05 was considered statistical significant.

## RESULTS

A total of 17 eyes (70,6% right eyes, 12 eyes) of 17 patients with large MHs who underwent ILM IFT were studied.

The mean age of the 17 patients was 63.24 ± 15.09 years, with a predominance of males (9 eyes, 52.9%). The mean follow-up was 7.76 ± 2.22 months, ranging between 6 and 12 months.

All eyes had large MHs with complete posterior vitreous detachment (old stage 4 MHs). The majority of cases were primary MHs (76,5%, 13 eyes) with the exception of 2 traumatic and post-vitrectomy MHs (both 11,8%). Relatively to MHs dimensions, the mean minimum and maximum diameters were, respectively, 578,5 ± 147,1µm and 1004,1 ± 254,6µm. Mean MH duration (82,35%, 14 eyes), evaluated

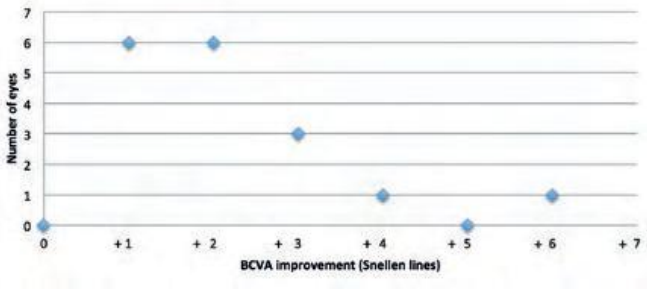


**Fig. 2 | BCVA variation (Snellen lines) at the mean follow-up time after the ILM IFT.** The percentage of eyes gaining one, two, three, four and six lines of BCVA were, respectively, 35,3%, 35,3%, 17,9%, 5,9% and 5,9%. Improvement from CF to 0,05 was considered as an improvement of one line.

by the duration of the patient's complaints, was 35,86 ± 40,33 months, being superior to 1 year in 47,1% (8 eyes). MH duration was unknown in 17,65% (3 eyes).

According to lens status, 47,1% (8 eyes) were phakic and with clear media, 11,8% (2 eyes) had cataract and 41,2% (7 eyes) were already pseudophakic. Combined surgery with cataract phacoemulsification was performed in 47,1% of cases (8 eyes), with the exception of 2 of the phakic eyes without cataract.

All surgeries were uneventful with the exception of one case of an iatrogenic peripheral retinal tear that was successfully treated with endolaser. No cases of free flap occurred, namely during the cutting of the ILM flap with the vitrectome, during its inversion into the MH or during the fluid-air exchange.

After a mean follow-up period of 7,76 months, closure rate was of 100% and all MH closed with a "U-shape" foveal morphology (Fig. 1). No cases of flat-open MH occurred. BCVA improved from 1,20 ± 0,48 to 0,68 ± 0,36 logMar units (approximately from 1/10 to 3/10 in Snellen decimal scale), which was statistically significant ($p<0,05$). All eyes improved their BCVA and 64,7% (11 eyes) gained two or more Snellen lines of BCVA. The percentage of eyes having at least BCVA of 2/10 was 23,5% (4 eyes) and 71,4% (10 eyes), respectively, in the preoperative (range CF-2/10) and in the postoperative period (range 1/20-8/10).

## DISCUSSION

We proposed to evaluate retrospectively the efficacy and safety of the ILM IFT in the treatment of large MHs. Large MHs represent a true surgical challenge, since both anatomic[6, 18, 19, 21] and functional[6, 10, 19] successes are more difficult to achieve.

Conventional ILM peeling aided by vital dyes was an important landmark in MH surgery and its usage in association with gas tamponade is widespread. Although closure rates superior to 90% can be found in the literature case-series[1, 2, 3], not only some MHs don´t close with this technique[19], but also the functional gains in BCVA in relation to vitrectomy without ILM peeling are controversial[20]. In fact, a "flat-open" outcome was commonly considered a surgical success, despite being associated with a poor visual outcome[19]. With the exclusion of "flat-open" MHs, a global closure rate of 85,7% was found in the EVRS MH Study, and of 78,2% in complete MHs with complete posterior vitreous detachment (old stage 4 MHs), independently of its size[6]. Minimum MH diameter seems to be particularly important in both anatomic and functional outcomes, with the closure rate (excluding flat-open outcomes) around 75% between 400 and 500µm and inferior to 50% above 500µm[19].

Our sample included only large MHs. The mean minimum diameter was 578,5 ± 147,1µm, being bigger than 500µm and 600µm in 71,6% and 41,2% of the cases, respectively. Other important features that contribute to the bad prognosis of this sample are the long duration of symptoms, with a mean value of almost 3 years, the presence of 4 cases of secondary MH (23,5%) and the low mean BCVA preoperative value (Table 1). Although concomitant cataract surgery, a predictor of a better postoperative BCVA, was performed in 47,1% of cases (8 eyes), only 11,8% (2 eyes) had cataract.

In this study, anatomic success was of 100%. Not only all MHs closed with absence of "flat-open" outcomes, but also all MHs closed in a "U-shaped" foveal configuration, associated with best visual outcome (Fig. 1). A moderate to evident restoration of both the ellipsoid band and the cone outer segment tips (COST) line was observed (Fig.1), as previously reported[9]. In fact, BCVA improvement from 1,20 ± 0,48 preoperatively to 0,68 ± 0,36 logMar units postoperatively was statistical significant. All eyes improved BCVA and 64,7% gained at least two Snellen lines. The ILM IFT, not only stimulates Muller cells, but also seems to act as a scaffold for tissue proliferation, resulting in an increased gliosis which seems to promote the centripetal migration of the perifoveal photoreceptors, improving both anatomic and functional success[16]. As BCVA seems to keep improving during the first year after surgery with the ILM IFT[7, 9], our results may also even improve.

These results, with closure rates around 100% and significant improvement in BCVA, are common in recent

**Table 1 | Preoperative characterization of the MH submitted to ILM inverted flap technique.**

| Parameter (unit) | Mean ± SD | Range (min/max) | Percentage / number of eyes |
|---|---|---|---|
| **Minimum diameter (µm)** | 578,5 ± 147,1 | 405/ 963 | --- |
| ≥ 500 µm | --- | --- | 71,6% / 12 |
| ≥ 600 µm | --- | --- | 41,2% / 7 |
| **Maximum diameter (µm)** | 1004,1 ± 254,6 | 479/ 1113 | --- |
| **Duration (months)** | | | |
| Known | 35,9 ± 40,3 | 1/ 132 | 82,4%/ 14 |
| < 12 months | --- | --- | 35,3% / 6 |
| ≥ 12 months | --- | --- | 47,1% / 8 |
| Unknown | --- | --- | 17,6% / 3 |
| **BCVA (logMar)** | 1,20 ± 4,85 | 0,52 / 2,00 | --- |

Abbreviators: SD- standard deviation; min- minimum; max-maximum.

case-series reports with the ILM IFT, even in extremely large MHs, where a free-flap did not occur and a complete peeling was not done inadvertently[14, 17]. Almost all eyes improve BCVA and even eyes that don't improve BCVA may have visual gains in visual field evaluated by microperimetry.

ILM IFT is a safe procedure. As a complication, we had a single case of a peripheral iatrogenic tear successfully treated with endolaser. ILM IFT most common complication is the occurrence of a "free-flap" which most often occurs during fluid-air exchange and that, in practice, results in a conventional complete ILM peeling[15]. No cases of free-flaps occurred in the eyes studied. In order to peel the ILM without losing it, apart from stopping ILM peeling before the hole edges and cutting the ILM flap with low aspiration to avoid detaching it, it is fundamental to minimize intraocular pressure variations. This can be achieved by the usage of valved trocars and low pressures during fluid-air exchange. Retinal nerve fiber layer damage causing paracentral scotomas as a consequence of the ILM peeling were not evaluated by multifocal electroretinography or microperimetry. However, in our opinion, its occurrence is not increased by the ILM IFT in relation to the complete conventional ILM peeling.

ILM IFT is until now a short history of success. Although we did exclude myopic MHs, ILM IFT has been used successfully, with a similar closure rate, in myopic MH in the absence of a concomitant foveoschisis or retinal detachment[17]. In its presence, in cases of extreme axial lengths, ILM IFT also seems to improve both anatomic and functional outcomes[13], being possible to associate it with macular indentation.

As a conclusion, we can say that ILM IVT is an effective and safe technique, which, in our opinion, represents a paradigm shift in large MHs surgery. In this study, with large MH with bad prognosis, the anatomic success rate was 100% and the gain in terms of functional BCVA was significant.

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