MICROPULSE LASER FOR MACULAR EDEMA

PRINCIPLES, NEW PARAMETERS AND RESULTS WITH 577 NM

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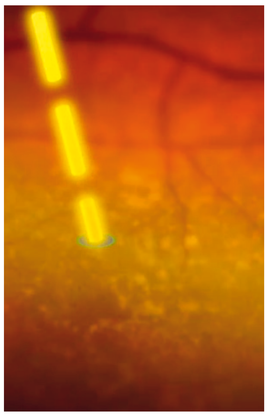
PURPOSE

The authors report their experience using 577 nm Micropulse Laser (MIP) in treatment of macular edema due to different pathologies.



METHODS

The study is a retrospective clinical trial evaluation (between February 2011 and June 2013) of sub threshold laser treatment as a tissue-sparing laser photocoagulation for ME.

83 eyes from 64 patients (29-92 years of age, mean 69) underwent treatment for ME due to Diabetic Retinopathy (55 eyes - 66,26%), branch (10 eyes- 12,05%) or central retinal vein occlusion (12 eyes- 14,46%) , or other causes (6 eyes- 7,23%) including inflammatory diseases (Birdshot) . (100 eyes from 75 patients were treated, but 17 eyes excluded for follow-up < 6 months). (*Table 1*)

53% had a glaucoma, with bi or tritherapy, often related with previous triamcinolone intravitreal injection.

Majority of patients had several and multiple previous treatments for their ME :

- 67 eyes (80,72%) had previous IVT (1 to 14), with bevacizumab alone (5 eyes), triamcinolone alone (9 eyes), or combined (53 eyes). Majority of patients had multiple IVTs (combined or not)
- 58 eyes (69,88%) had previous vitrectomy with ILM peeling
- 68 eyes (81,93%) had previous (grid or focal - modified or classic EDTRS) macular photocoagulation with conventional 532 nm

ME was quantified and followed up by OCT + Fluorescein angiography. Mean follow-up 20,8 months, range 6-31.

MIP diode laser used was the Supra Scan 577- Quantel Medical. Dye yellow laser (577 wavelength) offer the safer possibilities for treatment close to the fovea (quite no absorption by xantophyll pigments). MIP deliver the energy in succeeding train of very short pulses, with alternative « Laser on » and « Laser off= zero energy » phases (duty cycle = d/c).Because target is clearly RPE and avoid thermal effect of classic laser procedure, challenge is to use the lower d/c and keeping an effective laser treatment for ME. Main point is making no visible scars (corresponding to minimal collateral retinal damage) during the procedure and long time after too.

Treatment parameters for our MIP study were 100-120 µm spot size, 15% d/c for half patients, and 9% d/c for others. Number of spots varied from 80 to 750 (mean 450), Power from 300 to 500 mw (mean 410). We didn't use the multispot function allowed by Supra Scan. Spots were non confluent but dense, up to 250 µm from center of foveal avascular zone (FAZ) , numbers depending of clinically significant ME area to cover. Because we didn't used a 5% d/c, we applied a test laser burn in an area of non-edematous retina with continuous-wave emission mode, then adjusted power by doubling power in MIP mode. During the procedure, if we saw any tissue response, we decreased power from 20%, keeping the same d/c.

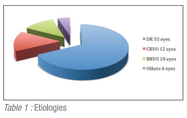


Table 1 : Etiologies

RESULTS

- Majority of patients (85,55%) had significant decrease in central mean thickness (CMT) with OCT (Cirrus or Heidelberg) .
- Visual acuity (Snellen VA chart) improved in 22,90%: 15,67% had 2 lines vision gain, 6,02% had 3 lines, and 1,21% 4 lines
- 62,65% obtained VA stabilization (+/- 1 Snellen Line) : 20,49% had 1 line vision gain, 36,14% remained unchanged, and 6,02% had 1 line vision loss.
- VA decreased in 14,45% : 9,63% had 2 lines vision loss, 2,41% had 3 lines loss, and 2,41% 5 lines loss.
- Several procedure were sometimes necessary (25 eyes - 30,12%) especially in DR (13 eyes - 52% of retreatment) . (*Table 2*)
- Mean delay between 2 MIP was about 3 months.
- A lot of eyes treated with 15% d/c had some minimal scars after 3 or 6 months on fundus infrared or autofluorescence (FAF), mainly on areas where ME was less important, and always far from FAZ. Few eyes with 9% d/c had such scars.

	CRVO	BRVO	RD	Others
1 MIP	8 eyes	5 eyes	42 eyes	3 eyes
2 MIP	3 eyes	4 eyes	8 eyes	/
3 MIP	1 eye	/	4 eyes	/
4 MIP	/	/	/	3 eyes
5 MIP	/	1 eye	1 eye	/

Table 2 : Number of MIP related to etiology

CASE 1

MALE, 55 YEARS OLD
BIRDSHOT RETINOPATHY

2009 >

ME (628 microns) left eye from May, right eye (575 microns) from August.

Subtenon triamcinolone LE, but associated with severe increase of IOP.

2010 >

Vitrectomy with ILM peeling both eyes with significant central macular thickness (CMT) decrease for LE, but no effect for RE. Visual acuity maintained to 5/10 RE and 6/10 LE

Anti-VEGF IVT (Bevacizumab) RE with ME decrease (500 to 376 microns) and VA improved to 7/10 seven months after. LE improved with time too (7/10, twelve months after ILM peeling, no ME recurrence).

2011 >

ME (RE 650 microns, LE 470 microns) and VA decrease (5/10), both eyes : Anti-VEGF IVT(Bevacizumab) . No effect. No driving possibility.

Anti-VEGF IVT(Bevacizumab) + subtenon Bethamethasone acetate for RE : No effect. Quite no reading capability.

2012 >

MIP three procedures (January, April, September) both eyes RE (250 i/450mw/15% - 180i/460 mw/15% - 250 i/500 mw/9%).

LE (225i/400 mW - 180i/460 mw/15% - 250 i/500 mw/9%)

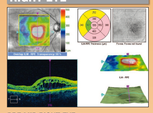
Significant improvement in CMT and VA, progressively.

2013 >

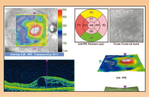
No ME both eyes (RE 238 microns - LE 254 microns). Some minimal scars (RE) in temporal macular area where ME was minimal. No change on fundus autofluorescence (FAF) or infrared SLO images for LE.

VA 7/10 RE , 6/10 LE. Normal reading capability, and driving car became again possible. 18 months from first MIP, 10 months from the last.

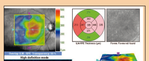
RIGHT EYE



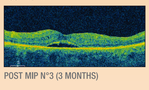
PRE MIP RIGHT EYE



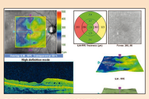
POST MIP N°1 (2 MONTHS)



POST MIP N°2

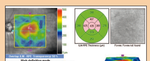


POST MIP N°3 (3 MONTHS)

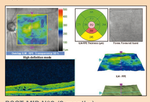


POST MIP N°3 (10 MONTHS)

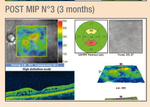
LEFT EYE



POST MIP N°2



POST MIP N°3 (3 months)



POST MIP N°3 (10 months)

CASE 2

MALE, 59 YEARS OLD
CRVO RIGHT EYE

2004 > ME (> 500 microns) and VA decreased to 3/10.

Vitrectomy with ILM peeling combined with Triamcinolone IVT N°1 with moderate central macular thickness (CMT) decrease. VA decrease to 2/10.

Triamcinolone IVT N°2 with ME decrease and VA improved to 4/10 one month after. Stabilized for 5 months but ME recurrence, VA 3/10 and Triamcinolone IVT N°3. ME decreased but severe increase of IOP, controlled with medical bi-therapy.

2005 > ME recurrence and VA 1/10. Cataract surgery and Triamcinolone IVT N°4. ME CMT decreased and VA 3/10.

2006 : ME huge recurrence (>600 microns), and VA 1/10. Triamcinolone IVT N°5 (March) and N°6 (November). No effect.

2007 > Anti-VEGF IVT(Bevacizumab) N°1 (January) with transient effect on CMT (488 microns). VA 2/10

ME increased (535 microns), VA 1/10 : Anti-VEGF IVT (Bevacizumab) N°2 (April) with combined subtenon Triamcinolone. Anti-VEGF IVT(Bevacizumab N°3 (December) with combined subtenon Triamcinolone : ME CMT 323 microns, and VA 2/10.

2008 > Anti-VEGF IVT(Bevacizumab) N°4 with combined subtenon Triamcinolone . No effect. ME 650 microns, VA 1/10.

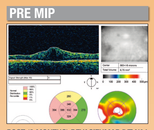
2009 > Conventional 532 nm Argon laser N°1. No effect. Anti-VEGF IVT(Bevacizumab) N°5. ME persistance in localized area (sup & central).

2010 > Anti-VEGF IVT(Bevacizumab) N°6 + subtenon Bethamethasone acetate . Quite no effect. Conventional 532 nm Argon laser N°2. No effect. ME (540 microns).

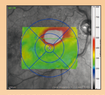
2011 > MIP (February and May) : 760 i/500 mw/15% - 400 i/450 mw/15%. ME decreased then disappeared. CMT 232 microns. VA 3/10.

2012 & 2013 > No obvious change (compared to previous images post 532 nm) on FAF or Infrared fundus images, except on temporal macula, with some minor scars (not on area with thicker ME). No ME recurrence after 26 months post MIP. VA maintained.

PRE MIP



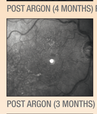
POST (3 MONTHS) BEVACIZUMAB IVT N°4 + TRIAM (2008)



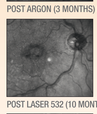
CASE 2 POST BEVACIZUMAB IVT N°5 (2009)

CASE 2 POST BEVACIZUMAB IVT N°5 (2009) SCAN

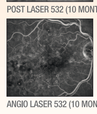
POST ARGON (4 MONTHS) PRE MIP AF



POST ARGON (3 MONTHS) PRE MIP IR



POST LASER 532 (10 MONTHS) 2009

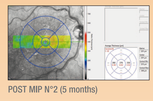


ANGIO LASER 532 (10 MONTHS) 2009

POST MIP

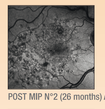
POST MIP N°1 (3 months) AF

POST MIP N°1 (3 months) IR

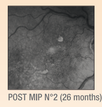


POST MIP N°2 (5 months)

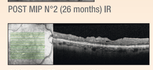
POST MIP N°2 (5 months) 2011



POST MIP N°2 (26 months) AF



POST MIP N°2 (26 months) IR



POST MIP (26 months) SCAN

CASE 3

FEMALE, 80 YEARS OLD
DR BOTH EYES
PREVIOUS PANPHOTOCOAGULATION

2010 >

ME (> 500 microns RE - 400 LE) and VA decreased to 1/20 RE and 2/10 OG. No reading capability.

Anti-VEGF IVT(Bevacizumab) N°1 for RE. No effect for ME but VA increase to 1/10.

Subtenon Triamcinolone N°1 for LE. No change for VA, ME decreased.

Vitrectomy with ILM peeling combined with Triamcinolone IVT for RE and Subtenon Triamcinolone N°2 for LE (December). ME decreased (moderate for LE) for both. VA RE 1/20 and LE 1/10.

2011 >

RE : no ME. VA 2/10

LE : Vitrectomy with ILM peeling combined with Triamcinolone IVT (March). Transient ME decrease. Conventional 532 nm Argon macula laser treatment.. Anti-VEGF IVT(Bevacizumab) N°1 + subtenon Bethamethasone acetate . ME decreased and VA 2/10.

2012 >

MIP Both eyes 3 procedures(March, June and October)

RE : 400i/400 mw/15% - 300i/400 mw/9% - 200i/400 mw/9%.

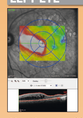
LE : 640i/410 mw/15% - 360i/500 mw/9% - 230i/500 mw/9%.

ME decreased.

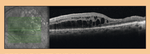
2013 >

No ME. No obvious change (both eyes) on FAF or Infrared images, compared to previous images (post ETDRS laser performed years before) VA 3/10 RE and 2/10 LE. Reading capability obtained. 10 months from first MIP, 6 from the last MIP.

LEFT EYE

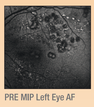


PRE MIP LEFT EYE OCT

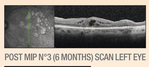


PRE MIP LEFT EYE SCAN

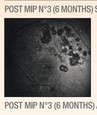
PRE MIP Left Eye IR



PRE MIP Left Eye AF



POST MIP N°3 (6 MONTHS) SCAN LEFT EYE

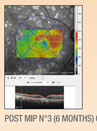


POST MIP N°3 (6 MONTHS) AF

RIGHT EYE

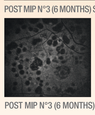
PRE MIP Right Eye IR

PRE MIP Right Eye AF



POST MIP N°3 (6 MONTHS) OCT RIGHT EYE

POST MIP N°3 (6 MONTHS) SCAN RIGHT EYE



POST MIP N°3 (6 MONTHS) RIGHT EYE AF

CASE 4

FEMALE, 68 YEARS OLD
BRVO SUPERIOR RIGHT EYE

2005 >

ME (> 650 microns) and VA : 1/20.

Focal 532 nm Argon laser treatment N°1 is performed : VA 1/10 and moderate decrease ME.

Vitrectomy with ILM peeling combined with Triamcinolone IVT N°1 : Good effect on ME and 2 months post-op : No ME and VA 5/10 with reading capability.

4 months post-op : ME recurrence and VA decreased to 3/10 : Triamcinolone IVT N°2. ME decreased but cataract.

2006 >

Cataract surgery. VA 7/10. No ME. 7 months post cataract surgery : ME recurrence and VA 3/10.

2007 >

Triamcinolone IVT N°3. ME decreased but IOP increased, controlled by medical bi-therapy. VA 5/10, then 2/10. Selective laser trabeculoplasty for glaucoma.

2008 >

ME increased : Focal 532 nm Argon laser treatment N°2. No effect.

ME 613 microns CMT : Anti-VEGF IVT(Bevacizumab) N°1. Good effect on CMT (ME 384 microns) and VA 5/10.

2 months post Anti- VEGF IVT : ME recurrence. VA 3/10: Anti-VEGF IVT(Bevacizumab) N°2 (October) VA 5/10. ME decreased ++.

2009 >

ME severe recurrence. VA 1/10 (January) : IVT(Bevacizumab) N°3 : No ME and VA 4/10 (February).

ME severe recurrence. VA 1/10 (March)

Vitrectomy with ILM peeling + Dye N°2 : VA 4/10 but ME resistance after 6 months post-op.

IVT(Bevacizumab) N°4. VA 3/10. ME resistance.

Focal 532 nm Argon laser treatment N°3. ME decreased, VA 5/10.

2010 >

ME moderate but VA 6/10.

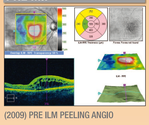
2011 >

ME increased : MIP one procedure (140i/330 mw/15%) No ME and VA 8/10 with reading capability.

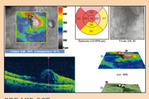
2012 & 2013 >

No ME recurrence after 24 months post MIP. A few scars on Infrared images / upper macula where ME was thinner. VA unchanged 8/10.

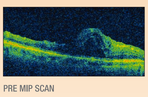
PRE MIP



(2009) PRE ILM PEELING ANGIO

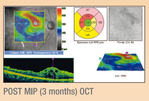


PRE MIP OCT

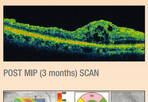


PRE MIP SCAN

POST MIP



POST MIP (3 months) OCT



POST MIP (3 months) SCAN

POST MIP (24 months) OCT

POST MIP (24 months) SCAN

DISCUSSION

Withboth 15% d/c and 9% d/c, MIP was associated sometimes with some scars, in areas where edema was less important. It seems to be quite a « millipulse » effect or nearly a modified ETDRS macular photocoagulation aspect. No extension of such scars was notified with follow-up, but it will need much more time to conclude for some patients. Moreover, reducing the d /c should resolve this adverse effect.

For some patients, several MIP procedures were patently obvious. But for a lot of patients (and we must say, majority), we took time to determine that a second or a third MIP was necessary. That is just to say that using MIP must be associated with reasoning, pragmatism, patience and « bon sens ». Perhaps we forgot it a little with oversimplicity of multiples IVTs… Majority of our patients had a long history, with multiple edemas recurences. We think possible that in the future, without such chronic ME, efficiency of MIP could be better, and VA improvement higher.

For patients with VA decreased, half had severe vision loss for Glaucoma, and half central scotoma for diabetic retinopathy with macular ischemia. (None because of MIP).

Surprisingly, MIP sometimes was very effective for some patients when all other treatments failed before (ILM peeling, conventional laser coagulation, multiple anti VEGF or corticosteroids intravitreal injections…) : for such patients, in the future, MIP should be considered. Moreover, we can imagine for patients with a new ME (without previous treatment), combined therapy. For example, one IVT first, then MIP. Same option could be done with ILM peeling, then MIP. Because MIP don't have some risks associated with surgery and IVTs, association with it should be interesting for patients, and safer, especially high rate of recurrence probability with ME. We can imagine that improving guide lines of MIP will lead us to use it a lot, with the strong argument that MIP could be done several time, without adverse effects for patients.

CONCLUSIONS

MIP seems to be effective for treating ME from different etiologies, sometimes when surgery, Corticosteroids or anti-VEGF injections failed. It allows an interesting choice for the future as a new approach for ME treatments.

It could be a an ajunctive treatment for reducing the number of intravitreal injections, or to combine with other procedures such as internal limitant membrane surgery. Duty cycle must be reduced to the lower level as possible, probably to 5% or close to.

Our study shows that it was difficult to begin first with a very low d/c, because the risk was clearly not being effective on eyes with chronic and resistant macular edema. Experience surely will lead us to performing MIP with combined safety and effectiveness. Improving guide-lines for using MIP better remains still a challenge.

Even if IVTs with pharmacological agents advances are clearly the leader for ME treatments, we think that clinical research for MIP is fundamental for such chronic diseases. And really, how many IVTs are bearable for patients ? Perhaps it is time to think and find other combined therapy.