
TRANSPUPILLARY THERMOTHERAPY (TTT): A novel approach in the treatment of occult subfoveal choroidal neovascularization in age-related macular degeneration (ARMD).

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INTRODUCTION:

ARMD is a leading cause of central vision loss in patients older than 50 years of age. The majority of eyes suffer severe vision loss as a result of choroidal neovascularization, the only proven effective treatment for which is laser photocoagulation.

The Macular Photocoagulation Study¹ demonstrated that treatment of well-defined subfoveal choroidal neovascularization was beneficial, but most patients experienced an immediate decline in vision because of damage to the overlying neurosensory retina.

Freud et al² demonstrated that only 13% of patients with choroidal neovascularization from ARMD are eligible for treatment by the MPS criteria, as the majority of patients present with occult choroidal neovascularization.

TTT represents an emerging new treatment for ARMD patients presenting with subfoveal occult choroidal neovascularization, who are currently untreatable with conventional techniques.

First described by Oosterhuis et al³ in 1995, in the treatment of choroidal melanomas, transpupillary thermotherapy is a technique in which heat is delivered to the choroid and retinal pigment epithelium through the pupil using a modified diode laser. This laser technique has been successfully used in the treatment of small choroidal melanomas. It is now being studied as a treatment modality for occult subfoveal choroidal neovascularization.

Preliminary results show that TTT shows no side effects and may be effective in treating occult choroidal neovascularization, in ARMD.

TECHNIQUE:

TTT is delivered through a slit lamp using an anti-reflective Goldmann contact lens and an infrared diode laser at 810 nm, specially modified to give a long pulse mode. The slit lamp has a special large spot size adapter with an adjustable beam width of 0.5 mm, 0.8 mm, 1.2 mm, 2.0 mm and 3.0 mm.

The treatment is given using one spot that encompasses the entire lesion. Laser parameters used are duration of 60 seconds, at power settings between 250 and 1000 mW, depending upon the spot size used. In general, for a 3 mm spot size, the initial power setting is 800 mW and is appropriately reduced for smaller spot sizes by keeping the power density around 10 W/ sq.cm. While treating densely pigmented eyes, the power setting needs to be reduced further. The end point is an area of no visible colour change to a light grey appearance. Full treatment results are usually seen within 2-3 months after the procedure.

DISCUSSION:

Conventional laser treatment for choroidal new vessels uses very strong laser power; hence, the closure of blood vessels may have as a counterpart the destruction of the overlying retina. In contrast to this, TTT, by creating a localized hyperthermia minimizes tissue coagulation to the surrounding tissues and the deep penetration to the choroid and retinal pigment epithelium can be optimized.

The infrared irradiation is beneficial as tissue penetration is high and absorption by ocular media is minimized^{4,5}. The large spot size is advantageous in that, large areas of occult choroidal neovascularization, can be treated and the increased diameter of the irradiation beam allows for minimal heat dissipation to the surrounding tissues⁶.

Histologic studies of TTT- treated choroidal melanomas show extensive thrombosis of tumor vessels after treatment. In a study by Journee-de Korner et al⁷, human eyes enucleated after TTT were examined, and thrombosis of tumor vessels was observed, perhaps explaining the low tendency of bleeding after TTT. In an analogous fashion, it is possible that this may be a mechanism by which TTT closes choroidal neovascularization in ARMD, resulting in faster cicatrization of the neovascular complex. This may limit subretinal exudation and macular edema, effectively reducing their damaging effects on the neurosensory retina and preserving visual acuity.

No patients have reported an acute loss of vision immediately following treatment. Occurrences of mild central scotoma and post-treatment edema have been reported. Even when this occurs, it is temporary and does not seem to affect the final visual acuity. No other complications have been observed.

In a pilot study conducted by Reichel E et al⁸, stabilization of vision occurred in 77% of patients and decreased exudation was seen in 94% of the patients having occult subfoveal choroidal neovascularization, who were treated using TTT.

Re-treatment can be considered not earlier than 12 weeks, if there appears to be minimal to no response to the treatment.

Clinical characteristics for re-treatment include:

- a) < 50% reduction in fluorescein leakage on FFA
- b) No flattening of pigment epithelial detachments
- c) No resolution of intraretinal and / or subretinal fluid
- d) No change in the elevation of the retinal pigment epithelium

OUR EXPERIENCE:

At our Institute, we conducted a prospective,

noncomparative study on a case series which included 19 eyes of 18 patients, with subfoveal occult choroidal neovascularization, who were treated with TTT.

MATERIALS AND METHODS:

All the patients in this study were 50 years of age or older and diagnosed with occult subfoveal choroidal neovascularisation secondary to ARMD. Patients had best corrected Snellen's visual acuities of 6/36 or less. Follow up period was ranging between 1-6 months with a mean follow up period of 4 months. TTT was delivered using the infrared diode laser at 810 nm, with a variable spot size of 0.5 mm, 0.8 mm, 1.2 mm, 2.0 mm, or 3.0 mm depending on the size of the choroidal neovascular membrane. The diode laser was delivered using a contact lens and the treatment was initiated in one spot for 60 seconds duration at a power range between 250-600 mW.

The end point was an area of no visible colour change to a light grey appearance.

In all eyes, the outcome was assessed by Snellen chart visual acuity and clinical examination in each follow-up visit.

RESULTS:

The results are as summarized below:

neovascularization.

One such prospective, randomized, placebo-controlled, multicentre clinical trial underway at present is the - Transpupillary thermotherapy (TTT) for choroidal neovascularization (CNV) Clinical Trial i.e. TTT4CNV Trial, sponsored by Iridex Corp. with its co-ordinating centre at the Tufts University School of Medicine, Boston.

REFERENCES:

- 1) Laser photocoagulation of subfoveal neovascular lesions of age-related macular degeneration. Updated findings from two clinical trials. Macular Photocoagulation Study Group. Arch Ophthalmol 1993; 111:1200-9.
- 2) Freund KB, Yanuzzi LA, Sorenson JA. Age-related macular degeneration and choroidal neovascularization. Am J Ophthalmol 1993; 115:786-91.
- 3) Oosterhuis JA. Journee-de Korver HG. Transpupillary thermotherapy in choroidal melanomas. Arch Ophthalmol 1995; 113:315-21.
- 4) Svaasand LO. Boerslid T. Thermal and optical properties of living tissue: application of laser-induced hyperthermia. Lasers Surg Med 1985;5:589-602.
- 5) Geeraets WJ. Williams RC. Chan G. et al. The loss of light energy in retina and choroid. Arch Ophthalmol 1960;64:606-15.

No of Eyes and/or patients	Length of follow up period	Outcomes		Complications
		Visual Acuity	Final exudative response	
19 eyes of 18 patients	1 to 6 months (mean: 4 months)	Improved: 2 eyes (13.3%) *Stabilized: 13 eyes (86.7%) Worsened: Nil (4 patients were lost to follow up after the procedure)	Decreased exudation 15 eyes (100%)	2 patients had subretinal bleed during the first follow up week, which resolved spontaneously. No other complications, or any other ophthalmoscopic or angiographic evidence of damage to the overlying retina was noticed in the other patients

*Stable: no change/ improvement of 1 line, in vision

CONCLUSION:

Thus, to conclude, TTT has been shown to effectively treat subfoveal occult choroidal neovascular membranes and preserve vision in patients with ARMD.

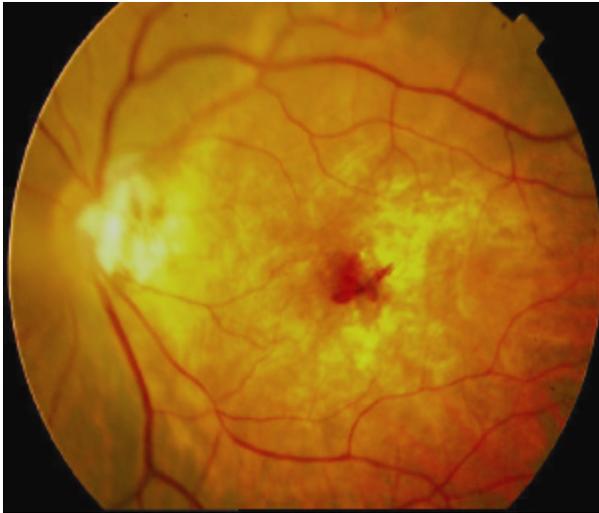
Randomized, prospective studies using larger number of patients will ultimately determine the role of TTT in the treatment of occult choroidal

6) L'Esperance FA. Technical considerations for ocular photocoagulation. In Klein EA (ed). Ophthalmic lasers. St.Louis.MO: CV Mosby CO. pp 78-113.

7) Journee-de Korver JG, Oosterhuis JA, Kemme H. Histopathological findings in human choroidal melanomas after transpupillary thermotherapy. Br J Ophthalmol 1997; 81: 234-9.

8) Reichel E, Berrocal AM, IP M, Kroll AAJ, Desai V, Duker JS, Puliafito CA: Transpupillary Thermotherapy of Occult Subfoveal Choroidal Neovascularization in Patients with Age-related Macular Degeneration. Ophthalmology 1999; 106:1908-14.

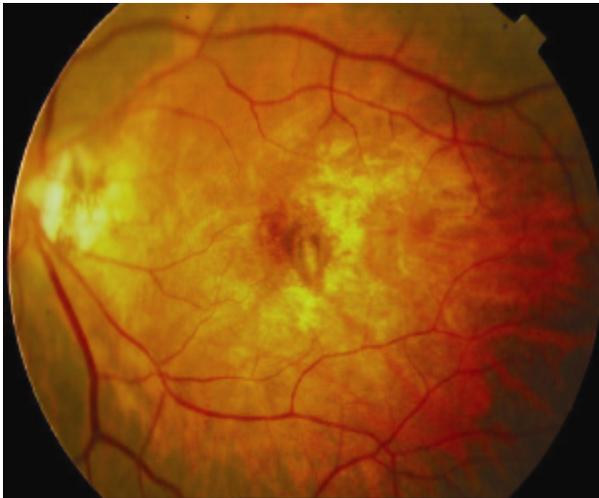
TRANSPUPILLARY THERMOTHERAPY (TTT)



1(a) LE ophthalmoscopy, before treatment, showing a myopic fundus with subfoveal haemorrhage.
LE vision - 6/24



1(b) LE fluorescein angiography, pretreatment, showing subfoveal leakage of the dye and blocked fluorescence due to haemorrhage from subfoveal SRNVM.



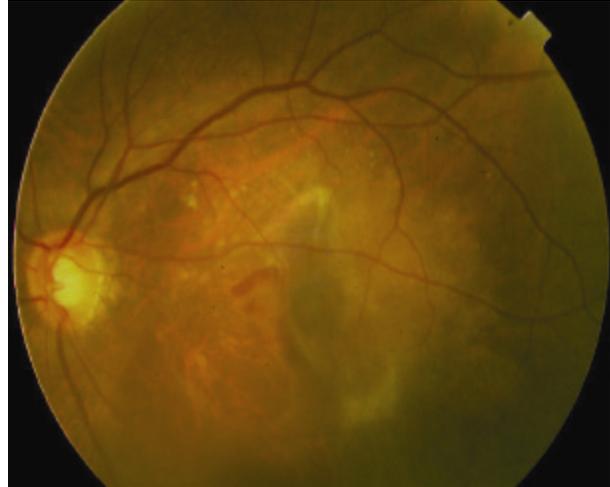
1(c) LE ophthalmoscopy, 4 months after TTT, showing reduced haemorrhage and scarring of the SRNVM
LE vision - 6/12



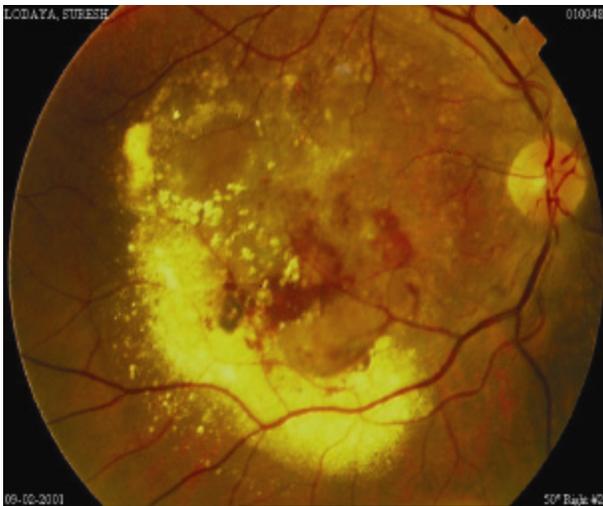
1(d) LE fluorescein angiography, 4 months post treatment, showing hypofluorescence due to scarring of the SRNVM.

TRANSPUPILLARY THERMOTHERAPY (TTT)

2(a) LE ophthalmoscopy, before treatment, showing a large subfoveal SRNVM with pigment epithelial detachment.
LE vision - 6/60



2(b) LE ophthalmoscopy, 4 1/2 months after TTT, showing a significant reduction of the pigment epithelial detachment and early scarring of the SRNVM.
LE vision - 6/36



3(a) RE ophthalmoscopy, before treatment, showing a large recurrent subfoveal SRNVM with subretinal haemorrhages and exudation. (The patient had previously received RE laser treatment elsewhere.)
RE vision - 6/60



3(b) RE ophthalmoscopy, 3 1/2 months after TTT, showing a significant reduction in the subretinal haemorrhages and exudation.
RE vision - 6/24