Safety and Utility of Local Chemotherapies using Melphalan for Eye-Preservation Therapy of Retinoblastoma

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Disclosure :

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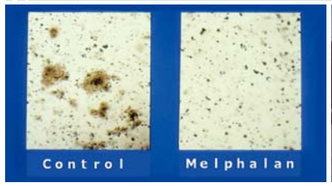
Background :

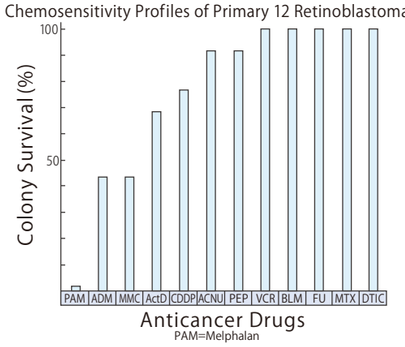
Because conventional eye-preservation therapies of retinoblastoma(RB) need new methods to increse the success rate, we developed local chemotherapies using melphalan (LCM) which was reported one of the most effective drugs to kill RB cells in vitro among 12 anticancer drugs. 1)

High Sensibility of RB to Melphalan discovered by Dr.Inomata



Dr.Inomata,M (National Cancer Center Research Institute)

Chemosensitivity Profiles of Primary 12 Retinoblastoma Cells



Purpose :

To make clear safety and utility of our LCM for eye-preservation therapy of RB(EPT)performed for 5 years from 2005 at our institution.

Cases and Methods :

Thirty eyes of 24 cases of RB which consisted of 17 eyes of R-E groups Ⅰ~Ⅳ and 13 eyes of R-E group Ⅴ. Our treatments involved 122 selective ophthalmic arterial injections using a balloon catheter(SOAI)[2],167vitreous injections using 32G needle at the pars plana(VI)[3] and 2 vitreous surgeries under perfusion of melphalan(VS)[4]. Our EPT was supported by conventional methos(TTT,Cryo,Ru-106,EBR) if necessary.

Result :

The success rare of EPT was 88% of R-E Groups Ⅰ~Ⅳ and 30% of R-E Group Ⅴ. Two eyes treated by VS needed enucleation due to recurrence. But neither orbital recurrence nor metastasis was found.

Conclusion :

Our LCM is safe and effective but further reinforcement is desirable.

References :

1) Inomata,M et al : Jpn J Cancer Research 1987;78:858-868
2) Yamane,T et al : Int J Clin Oncol 2004;9:69-73
3) Kaneko,A et al : Jpn J Clin Oncol 2003;33:601-607
4) Shimoda, Y et al : Graefes Arch Exp Ophthalmol 2008;246:501-508

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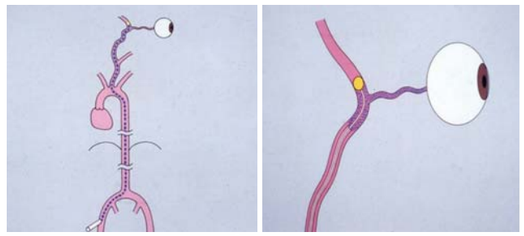
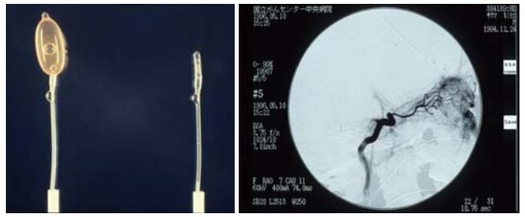
Selective Ophthalmic Arterial Injection developed by Dr.Mohri M,1987





Comparison of SOAI vs Systemic Chemo

	SOAI	Systemic Chemo
Drug	Melphalan	VEC*
Training	Special	Usual
Radiation Exposure	Little	No
Effect of Drug	Ocular Region	Full Body
Management	Easy	Not Easy
Loss of Hair or Leukopenia	Avoidable	Unavoidable
Days of Admission	4-6 days	Over 2 weeks
Days of Tx	9 weeks	24 weeks

*: vincristine , etoposide , carboplatin

Balloon Catheter Vs Direct Insertion

	Balloon	Direct
Dependence on the size of OA	No	Yes
Age (month)	More than 1	More than 6
Heparinizing	No	Yes
Infusion Time	10 sec.	30 min.
Wedging	No	Yes

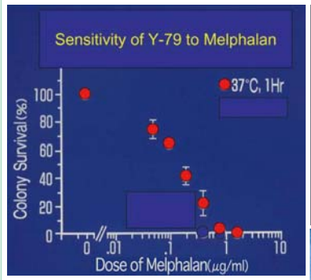
Safety of SOAI Toho University Ohashi Medical Center (2005~2010)

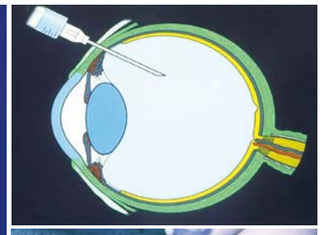
122 Injections for 29 eyes

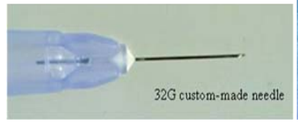
Disturbance of Retinal Artery*	4 (3.3%)
Temporary Lid Swelling	3 (2.5%)
Temporary Disturbance of Eye Movement	2 (1.6%)
Temporary Pancytopenia	1 (0.8%)
Postponement of Injection Due to Spasm of the ICA	1 (0.8%)

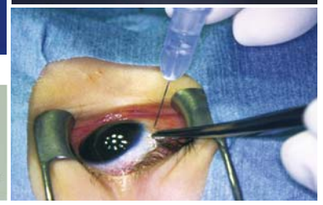
* Over dosage of melphalan was suspected.

Vitreous Injection of Melphalan

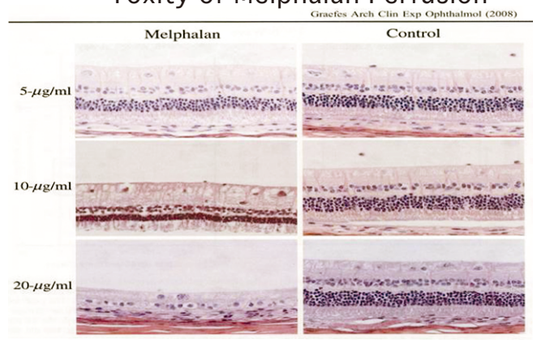




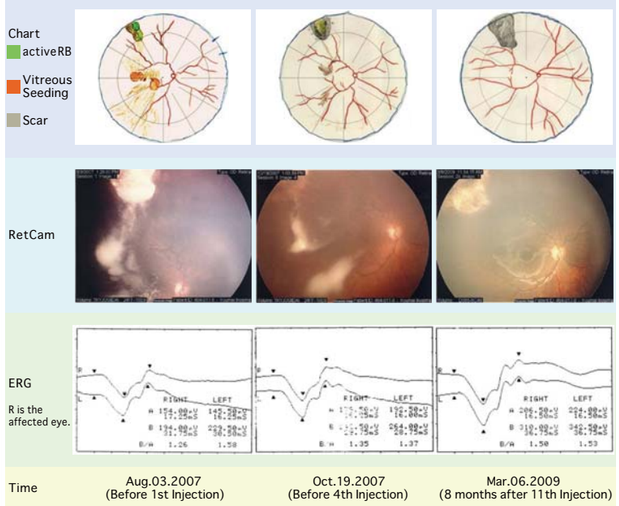




Toxity of Melphalan Perfusion



A case with Residual Massive Vitreous Seeding treated Successfully by 11 Times of Intravitreal Injection of Melphaln

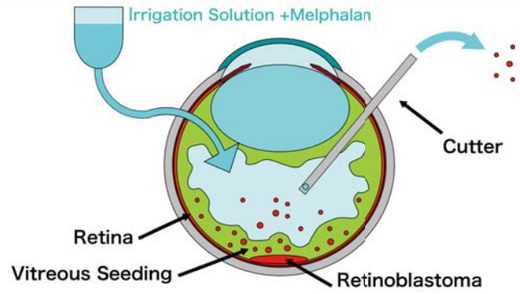


Safety of Vitreous Injection Toho University Ohashi Medical Center (2005~2010)

167 Injections for 21 eyes

Retinal tear	1 (0.6%)
Hyposphagma	1 (0.6%)
Extra-ocular extension or Metastasis of RB	0 (0%)

Eye-Preservation Therapy using Vitreous Surgery with Melphalan Perfusion

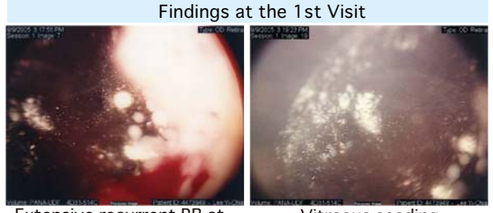


The 1st case of vitreous surgery with melphalan perfusion

2-year-old girl

Jul. 2004	diagnosed as Bilateral RB (Vb , R-E) treated by VEC (6 courses) and additional chemo.(CPA , DXR ,VCR) (3 courses)
Apr. 2005	EBRT(50Gy) to OU.
Jun. 2005	Cryo & TTT to OD.
Aug. 2005	Decreased Vision of OD due to vitreous hemorrhage & recurrence of RB. Referred to our hospital to be performed SOAI & VI of melphalan to OU.
Jul. 2006	Recurrence of OD treated by vitreous surgery with melphalan perfusion.

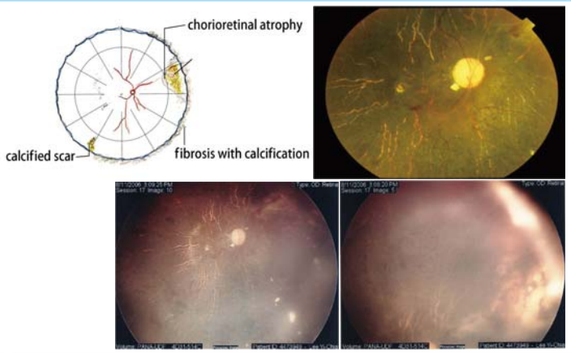
Findings at the 1st Visit



Extensive recurrent RB at the nasal periphery & VH

Vitreous seeding

No active RB with useful vision after the vitreous surgery (Aug.2006)



Recurrence & Enucleation (Nov.2006)