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OSPEDALE SAN RAFFAELE

DOSE-VOLUME PREDICTORS OF RADIO-INDUCED COMPLICATIONS AFTER RADIOSURGERY FOR UVEAL MELANOMA

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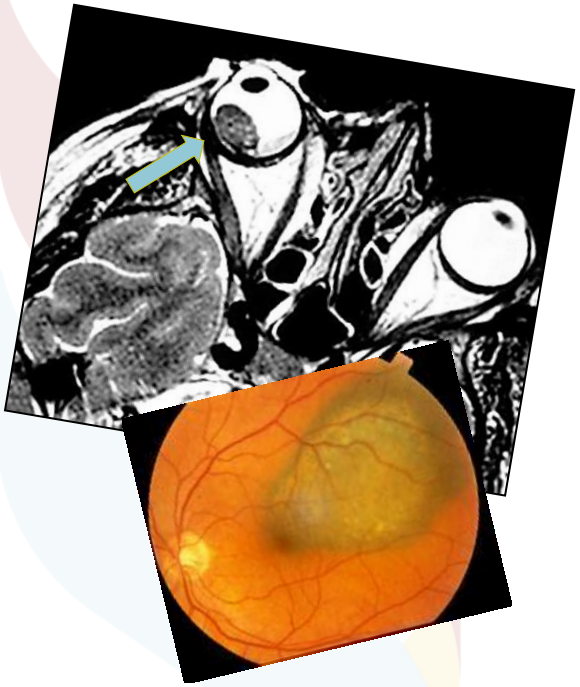
PURPOSE



- **Uveal melanoma** (UM) intraocular malignancy
- Highly aggressive → 40-50% overall mortality rate in 15 years

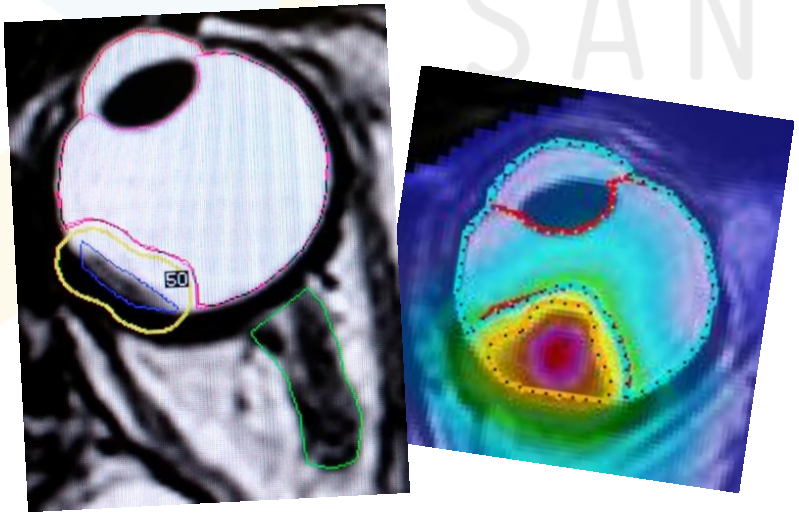
- **Gamma Knife stereotactic radiosurgery (GKRS)** → good *survival*, *local control* and *eye retention*
- *Complication rate* → ranging from 55% to 82%

→ To assess dosimetry and clinical variables associated with risk of radio-induced effects in patients affected by UM treated with GKRS

Clinical and dosimetric data

→ 66 pts treated with exclusive GKRS for UM enrolled

Anagrafic information, Clinical findings of tumor, Ultrasonography, Treatment information, DVHs (→Re-contoured critical structures on the MRI *)



*** Optic nerve, eyeball and posterior segment of the bulb**

End-points

- Ophthalmological examination before, 1 day, 1, 3 and 6 months after GKRS → then each six months
- Median FU = 2 years
- Toxicities with a n° of events > 6

Side effect	Incidence (%)	Median onset time (range) [months]
Radiation Vasculopathy	8/66 (12%)	24.8 (13.7-41.9)
Neovascular Glaucoma	7/66 (11%)	15.6 (11.8-37.1)
Radiation Papillopathy	7/66 (11%)	19.5 (12-41.9)
Subretinal Exudation	7/66 (11%)	18.7 (5.1-29.3)
Visual Acuity reduction ≥ 20%	42/66 (63.6%)	6 (6-24)
100% Visual Acuity reduction	15/66 (22.7%)	6 (6-36)

Statistical Anlyses

- **Kaplan-Meyer method** for actuarial risk
- **Two-sided t-tests** for preselection of the dose-volume parameters
- **Univariate and multivariate Cox's proportional hazard model**

•Receiver operating characteristic (**ROC**) curve to evaluate cut-off values of significant variables

•The area under the ROC curve (**AUC**) to measure discriminative power of models

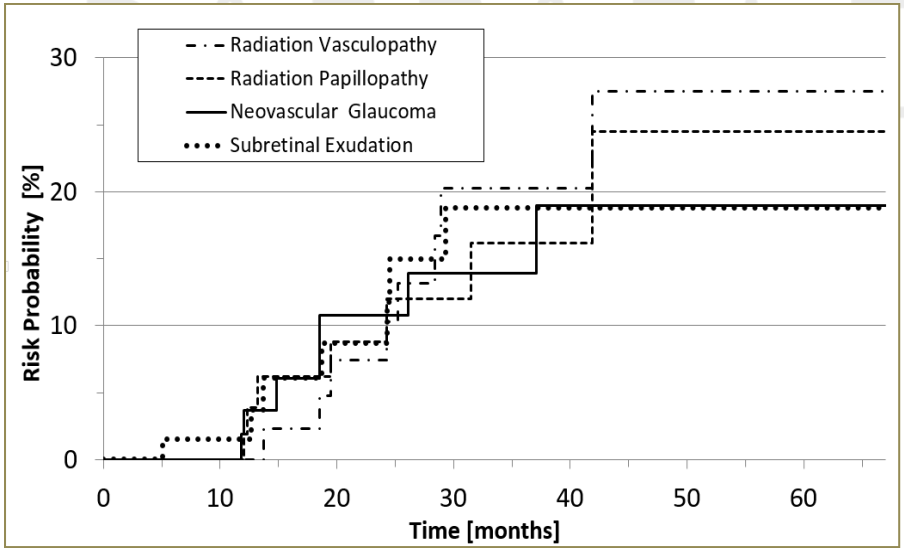
RESULTS

Univariate Cox's analyses of factors predicting GKSR-related toxicities

Predictive factor /end-point	Neo Vascular Glaucoma	Radiation Vasculopathy	Radiation Papillopathy
$D_{1\%}$ Optic Nerve		p=0.0009 HR=1.2 cut-off: 23.8Gy AUC=0.86	p=0.009 HR=1.14 cut-off: 14.9Gy AUC=0.83
V20 Posterior Segment	p=0.0003 HR=1.12 cut-off: 413.7mm^3 AUC=0.83		
Prescription Isodose - Optic Nerve Distance		p=0.0114 HR=0.33 cut-off: 2.2 mm AUC=0.87	
Position: anterior to equator		p=0.008 HR=0.14	
Tumor Thickness	p=0.0009 HR=2.01 cut-off: 8.7mm AUC=0.83		

Kaplan-Meyer actuarial risk probability → **2-years risk**

- NVG 14%
- RP 12%
- RV 10%
- SE 15%

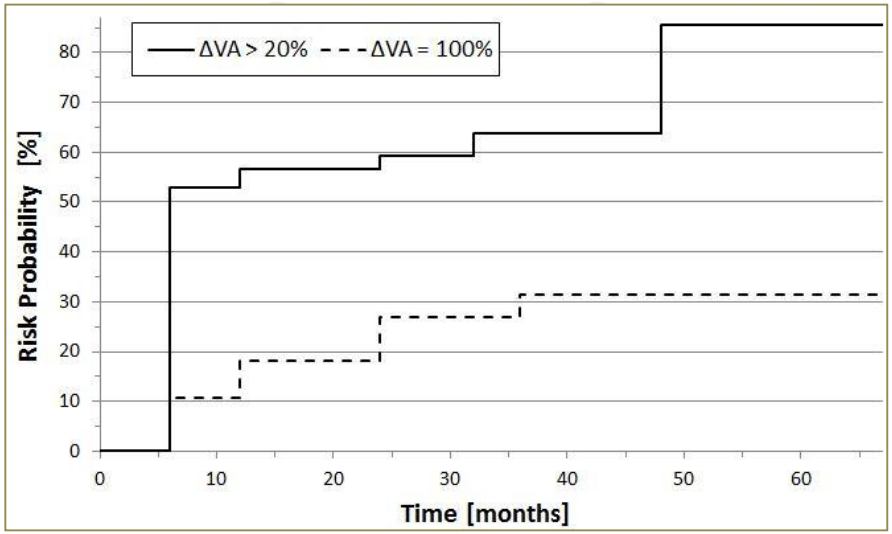


Multivariate Cox's analyses of factors predicting basal Visual Acuity reduction

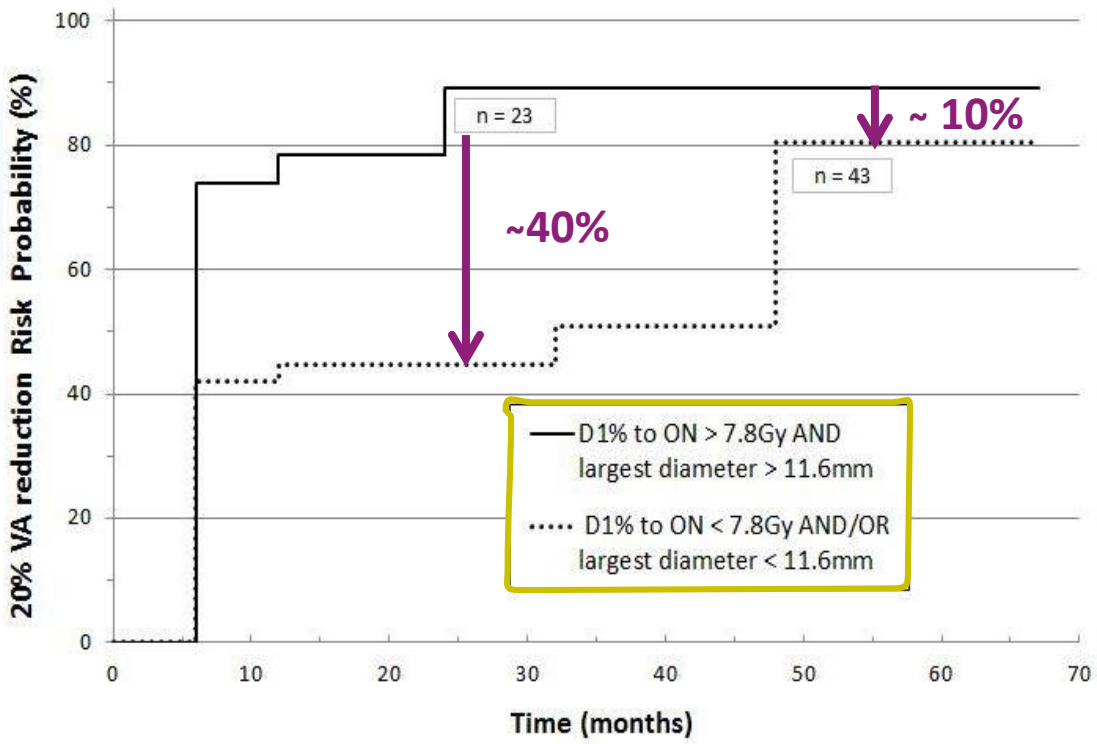
Predictive factor /end-point	20% basal VA reduction	100% basal VA reduction	
	Model : AUC=0.79	1° Model : AUC=0.83	2° Model : AUC=0.86
$D_{1\%}$ Optic Nerve	p=0.045 HR=1.04 cut-off: 7.8 Gy	p=0.002 HR=1.12 cut-off: 13.2 Gy	
Largest Tumor Diameter	p=0.02 HR=1.15 cut-off: 11.6 mm	p=0.007 HR=1.36 cut-off: 9 mm	p= 0.0035 HR=1.47 cut-off: 9 mm
Prescription Isodose - Optic Nerve Distance			p= 0.006 HR=0.56 cut-off: 3.9 mm

Kaplan-Meyer actuarial risk probability → **2-years risk** :

- ΔVA≥20% 59%
- ΔVA=100% 27%



KM risk probability for 20% VA reduction



- early reduction:

<u>double risk</u> for the population exceeding the cutoff values

- late reduction:

<u>risk comparable</u> → dose constraint effective in postponing the onset of VA reduction

KM risk probability for 100% VA reduction

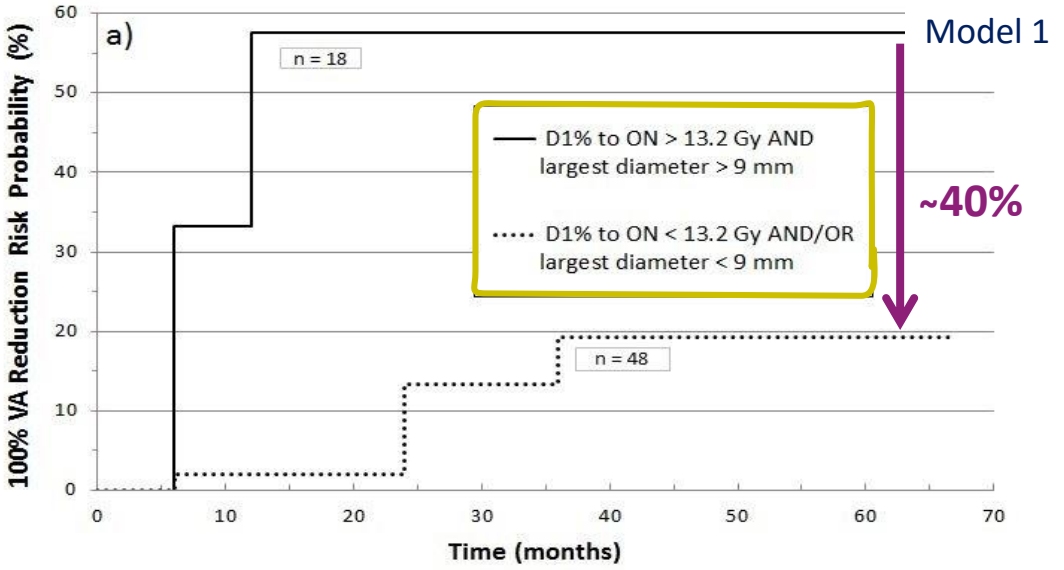
- 1st model:

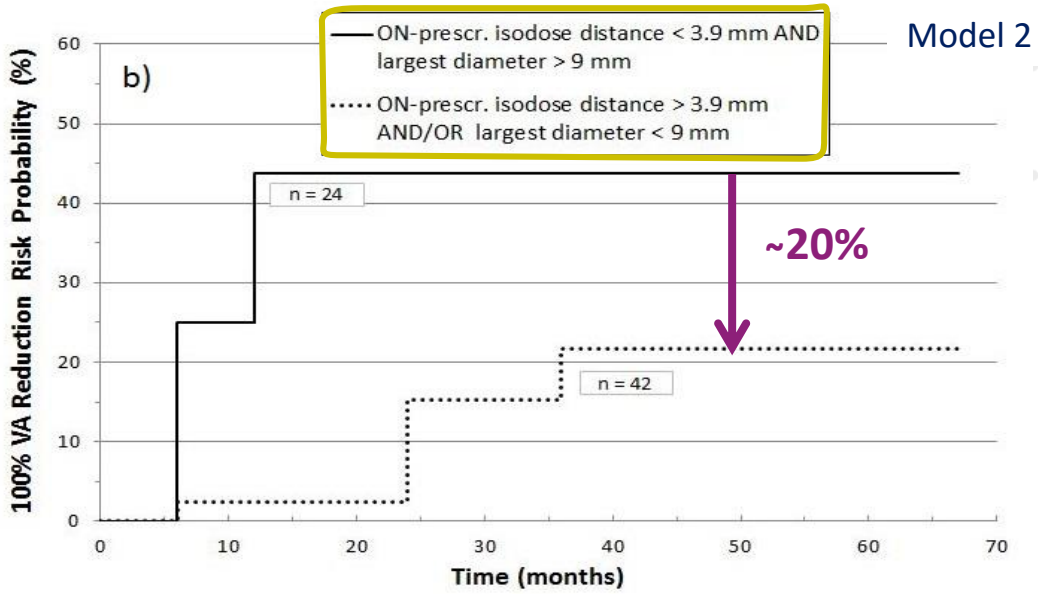
<u>risk 3 times higher</u> for the population exceeding the cutoff values

Dose constraint in line with the QUANTEC guidelines

- 2nd model :

influence of **dose conformation** to the target → constraint independent from the prescribed dose





CONLUSIONS

- ✓ Found **clinical and dosimetry variables** to clearly predict the risk of toxicities → dose constraints to critical structures
- ✓ Reducing **V20 of the posterior part of the bulb** → reduction of risk of glaucoma
- ✓ Constraining **D_{max} to the optic nerve below 12-13 Gy** → dramatic reduction of risk of blindness.
- ✓ **Tumor dimension** (LTD < 9-11 mm) → limitation for dose constraints implementation *to maintain the tumor local control*