COBRA project and predictive models interventional radiotherapy for uveal melanoma

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Gemelli
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ART
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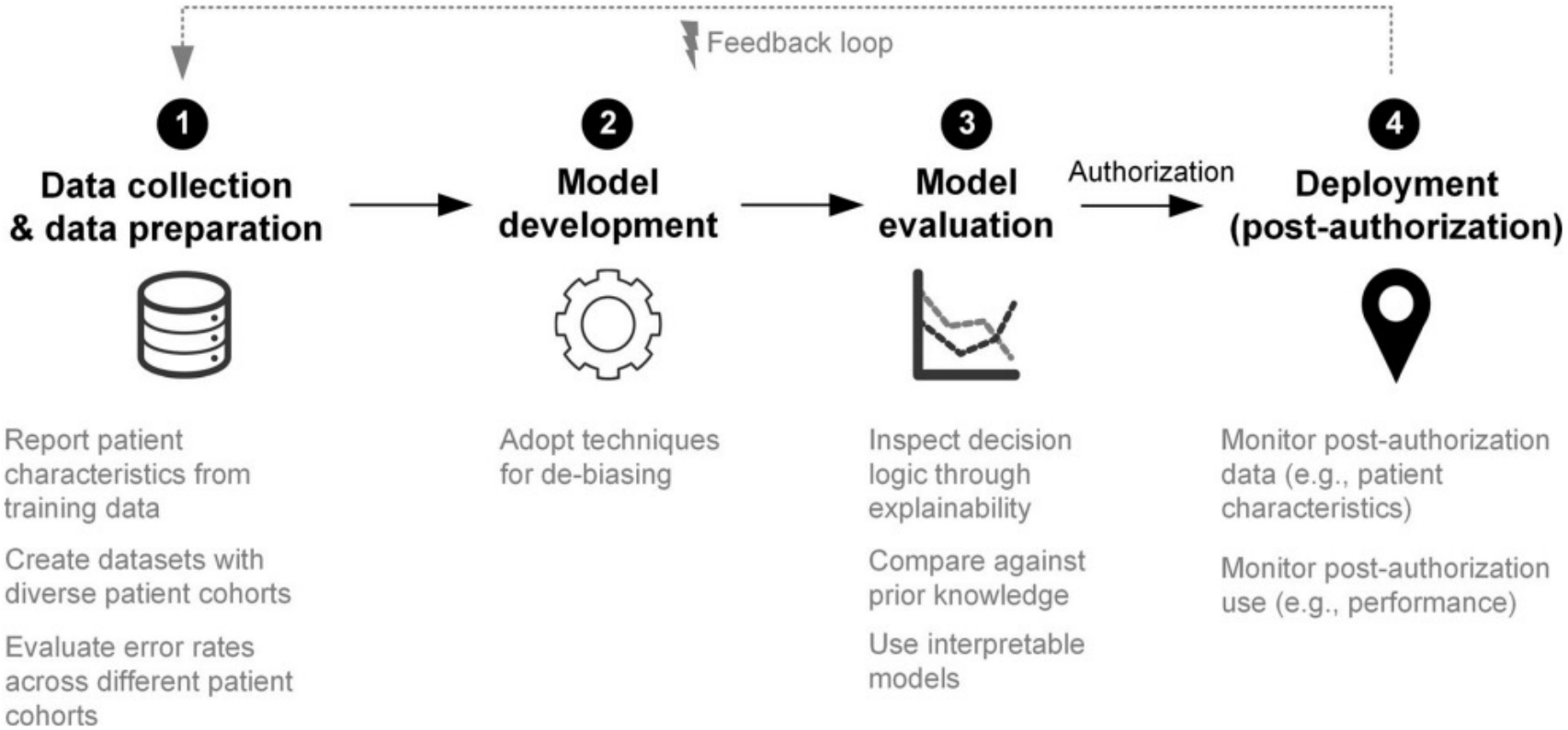


Fig. 1 Strategies for mitigating bias across the different steps in machine learning systems development. Diagram outlining proposed solutions on how to mitigate bias across the different development steps of ML-based systems for medical applications: (1) Data collection and data preparation, (2) Model development, (3) Model evaluation, and (4) Deployment.

Gemelli ART Advanced Radiation Therapy

Vokinger, K.N., Feuerriegel, S. & Kesselheim, A.S. Mitigating bias in machine learning for medicine. *Commun Med* **1**, 25 (2021)

Retrospective multicenter?

Prospcetive multicenter?

Review Articles

Review paper

ENT COBRA (Consortium for Brachytherapy Data Analysis): interdisciplinary standardized data collection system for head and neck patients treated with interventional radiotherapy (brachytherapy)

The H&N GEC-ESTRO WG approved the project in December 2012 and the text for the agreement was defined in March 2013.

Eleven centers from 6 countries signed an agreement and the consortium approved the ontology.

Review paper

ENT COBRA (Consortium for Brachytherapy Data Analysis): interdisciplinary standardized data collection system for head and neck patients treated with interventional radiotherapy (brachytherapy)

The Groupe Européen de Curiethérapie – European Society for Radiotherapy & Oncology Head and Neck Working Group (GEC-ESTRO H&N WG) started the H&N COBRA project approving its structure and defining:

1) the consortium agreement,

2) the ontology (data-set),

3) minimal requirements for each center to participate in the project.

Review paper

ENT COBRA (Consortium for Brachytherapy Data Analysis): interdisciplinary standardized data collection system for head and neck patients treated with interventional radiotherapy (brachytherapy)

Table 2. COBRA framework

The development and validation of multi-factorial prediction models requires the availability of a large amount of data pathology-bounded considered significant for present and futures studies
Each variable has to be included into a terminological system; adding more variable in the future is possible, if everything about the data is correctly specified (e.g. denomination, measurement units, measurement modality)
Collected data has to be reusable both in time (e.g. in the future) and in the space (across different institutions or research groups); reusability of legacy data is possible, at the condition that suitable semantic remapping functions from old to new data are provided
Appropriate mathematical and statistical methods are needed in order to learn from a large collection of data (Large Database) and help to suggest new modelling hypotheses to be tested
Patients privacy protection has to be protected; this can be accomplished in two ways: • by anonymizing data before they leave the collecting institutions walls, making sure that no inverse remapping is available ("cloud" solution) • by exploiting so called "Distributed Learning" solution, in which no data ever leaves the collecting institution but a regressive or classifying predictive model can be learned exactly as if all data had been collected in the same place

Review paper

ENT COBRA (Consortium for Brachytherapy Data Analysis): interdisciplinary standardized data collection system for head and neck patients treated with interventional radiotherapy (brachytherapy)

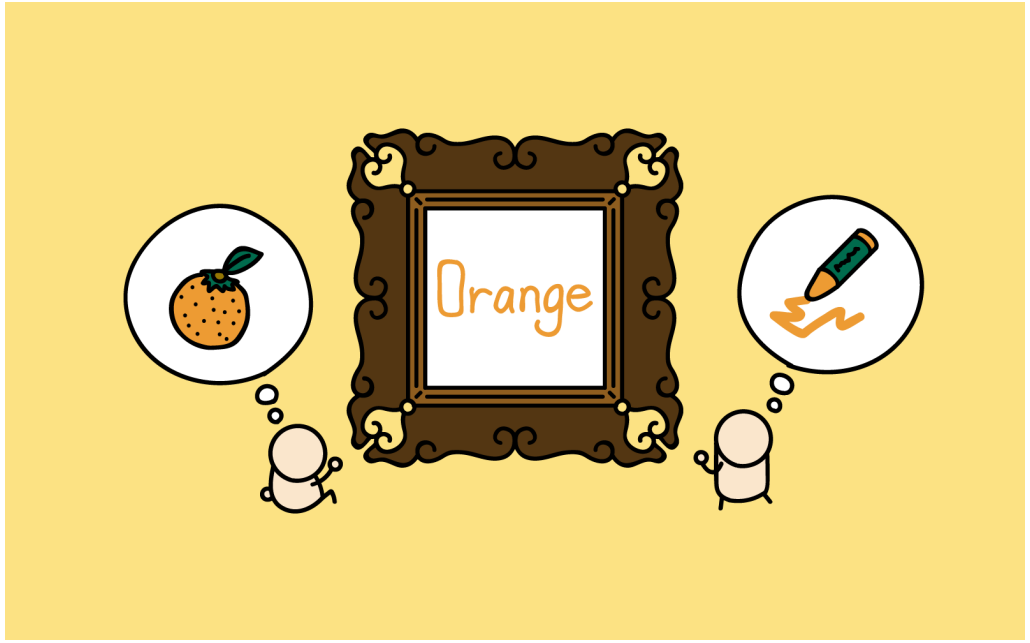


Table 3. Forms

1) Registry and history
2) Histology
3) Staging
4) Protocol
5) Surgery
6) Radiotherapy
7) Neoadjuvant chemotherapy (CT)
8) Concomitant CT
9) Adjuvant CT
10) Brachytherapy
11) Follow-up (repeated)
12) Outcome (automatically calculated based on follow-up)
13) Images and treatment files

Review paper

ENT COBRA (Consortium for Brachytherapy Data Analysis): interdisciplinary standardized data collection system for head and neck patients treated with interventional radiotherapy (brachytherapy)

Table 1. Minimal requirements of each Centre to participate to the COBRA consortium

In order to participate in the consortium, sign the agreement
To have an Electronic Medical Record (EMR) for brachytherapy to record patient's information
To be able to 'translate' local data into an ontology based archives
To be able to anonymize local data
To use technology able to developed advanced multicentre researches
To provide patient's written informed consents according to local national legislation

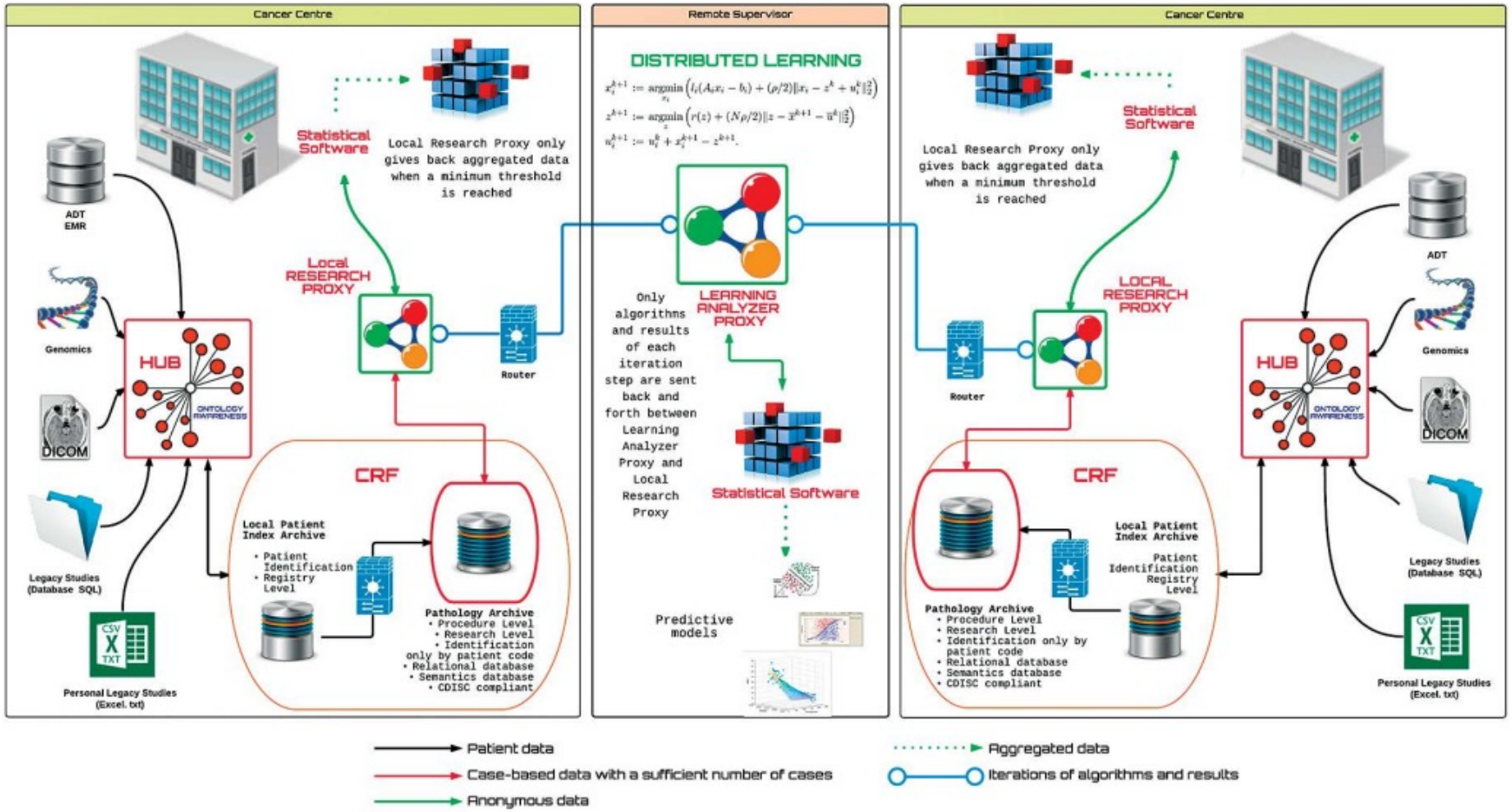


Fig. 2. BOA physically separates privacy relevant information from registry level data splitting this two pieces of information into two databases: "Local Patient Index Archive" and "Pathology Archive". It sends only clinical data to Cloud Large Database, destroying the inverse mapping, HUB (optional module of BOA) extracts and harmonizes legacy data while making them available for BOA, Local Research Proxy (optional module of BOA) makes local queries on its own pathology database. Learning Analyzer Proxy (module of BOA only in distributed mode) sends algorithms directly to Local Research Proxies, taking back from them only the results of each iteration step, with no need to work with shared data in the Cloud anymore. In this mode, Local Research Proxies do not move data around: they only apply iterative algorithms that the Supervisor will use to build consensus and estimate the model's parameters

Review paper

ENT COBRA ONTOLOGY: the covariates classification system proposed by the Head & Neck and Skin GEC-ESTRO Working Group for interdisciplinary standardized data collection in head and neck patient cohorts treated with interventional radiotherapy (brachytherapy)

The ontology was defined by a task group (LT, AB, GK), a technical commission (TeCo) composed by a mathematician (AD), an engineer (RG), a physicist with experience in data storage (JL), a physician with experience in data storage (ND), and a software expert (VL).

Review paper

ENT COBRA ONTOLOGY: the covariates classification system proposed by the Head & Neck and Skin GEC-ESTRO Working Group for interdisciplinary standardized data collection in head and neck patient cohorts treated with interventional radiotherapy (brachytherapy)

Two hundred and forty variables were defined on 13 input forms.

There are 3 levels, each offering a specific type of analysis:

1. Registry level (epidemiology analysis);
2. Procedures level (standard oncology analysis);
3. Research level (radiomics analysis).

ENT COBRA ONTOLOGY: the covariates classification system proposed by the Head & Neck and Skin GEC-ESTRO Working Group for interdisciplinary standardized data collection in head and neck patient cohorts treated with interventional radiotherapy (brachytherapy)

Brachytherapy technique value	# of occurrences	%
Interstitial	310	95.4
Intracavitary	15	4.6
Not available	0	0

Table 1. Number of occurrences and frequencies for 'gender' values in the cloud-shared database

Gender value	# of occurrences	%
Male	226	69.6
Female	98	30.1
Not available	1	0.3

Table 2. Number of occurrences and frequencies for 'histology type' values in the cloud-shared database

Histology type value	# of occurrences	%
Squamous cell carcinoma	272	84
Adenocarcinoma	19	6
Lymphoepithelioma	10	3
Soft tissue tumors and sarcomas	8	2.5
Basal cell neoplasms	7	2.1
Nevi and melanomas	4	1.2
Cystic, mucinous, and serous neoplasms	2	0.6
Blood vessel tumors	1	0.3
Mucoepidermoid neoplasms	1	0.3
Undifferentiated carcinoma	1	0.3
Not available	0	0

Cancer site value (ICD9)	# of occurrences	%
141 Malignant neoplasm of tongue	94	28.9
146 Malignant neoplasm of oropharynx	58	17.8
160 Malignant neoplasm of nasal cavities, middle ear, and accessory sinuses	40	12.3
161 Malignant neoplasm of larynx	35	10.8
147 Malignant neoplasm of nasopharynx	19	5.8
148 Malignant neoplasm of hypopharynx	16	4.9
144 Malignant neoplasm of floor of mouth	14	4.3
145 Malignant neoplasm of other and unspecified parts of mouth	12	3.7
173 Other malignant neoplasm of skin	9	2.8
172 Malignant melanomas of skin	6	1.8
142 Malignant neoplasm of major salivary glands	6	1.8
190 Malignant neoplasm of eye	4	1.2
171 Malignant neoplasm of connective and other soft tissue	3	0.9
143 Malignant neoplasm of gum	2	0.6
199 Malignant neoplasm without specification of site	2	0.6
153 Malignant neoplasm of colon	2	0.6
238 Neoplasm of uncertain behavior of other and unspecified sites and tissues	1	0.3
192 Malignant neoplasm of other and unspecified parts of nervous system	1	0.3
158 Malignant neoplasm of retroperitoneum and peritoneum	1	0.3
Not available	0	0

Review papers

Review paper

ENT COBRA ONTOLOGY: the covariates classification system proposed by the Head & Neck and Skin GEC-ESTRO Working Group for interdisciplinary standardized data collection in head and neck patient cohorts treated with interventional radiotherapy (brachytherapy)

European Journal of Internal Medicine 53 (2018) 73–78

Contents lists available at ScienceDirect

European Journal of Internal Medicine

journal homepage: www.elsevier.com/locate/ejim

Original Article

A new standardized data collection system for interdisciplinary thyroid cancer management: Thyroid COBRA☆

Clinical Investigations

Original paper

SKIN-COBRA (Consortium for Brachytherapy data Analysis) ontology: The first step towards interdisciplinary standardized data collection for personalized oncology in skin cancer

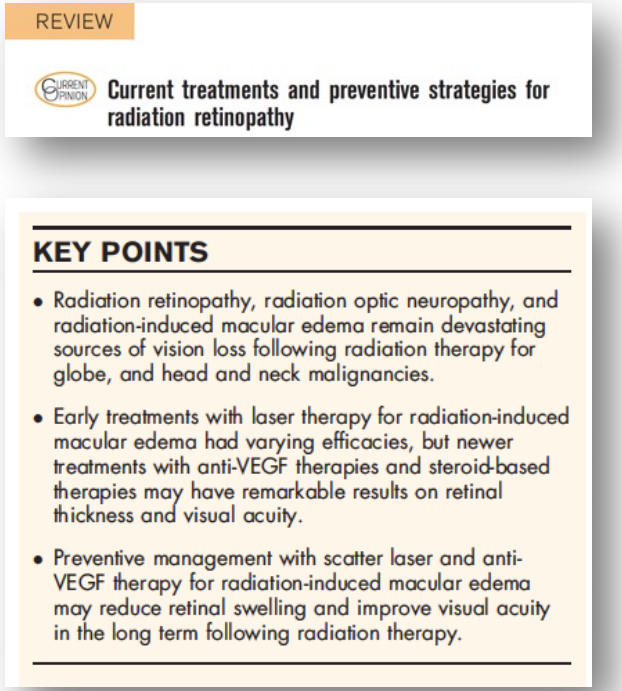
Gemelli ART Advanced Radiation Therapy

Radiation maculopathy complication is a frequent cause of losing reading vision in the irradiated eye

	Series characteristics			*2, 3, and 5 year cumulative probabilities of radiation related complications*				
Reference	*Type of irradiation**	*Large size† (%)*	*Anterior location‡ (%)*	*Cataract (%)*	*Neovascular glaucoma (%)*	*Vitreous haemorrhage (%)*	*Maculopathy (%)*	*Optic neuropathy (%)*
Char (1989)[12]	He				20, 27 ,—	7, 9, 15		
	I				6, —, —	17, 24, 28		
Char (1990)[8]	He	62	59	9, 27, 45	23, 30, 33			
Decker (1990)[13]	He		100		40, 43, 43			
Lindstadt (1990)[14]	He	66	22		26, 32, 36			
Guyer (1992)[16]	Pb	0	0				55, 69, 78§	
Kleineidam (1993)[17]	Co		62	21, 35, 57				
Quivey (1993)[18]	I	53	36	4, 14, 25		15, 22, 29		
Lommatzsch (1994)[19]	Ru		0					40, 55, 66**
								7, 10, 23††
Present series	Ru	56	38	21, 27, 37	4, 11, 21	10, 18, 27	15, 30, —	10, 12, —

Most probable complication

- Summanen P, Immonen I, Kivelä T, Tommila P, Heikkonen J, Tarkkanen A.Radiation related complications after ruthenium plaque radiotherapy of uveal melanoma. **Br J Ophthalmol. 1996**
- Takiar V, Voong KR, Gombos DS, Mourtada F, Rechner LA, Lawyer AA, Morrison WH, Garden AS, Beadle BM. A choice of radionuclide: Comparative outcomes and toxicity of ruthenium-106 and iodine-125 in the definitive treatment of uveal melanoma. **Pract Radiat Oncol. 2015**



REVIEW

Current treatments and preventive strategies for radiation retinopathy

KEY POINTS

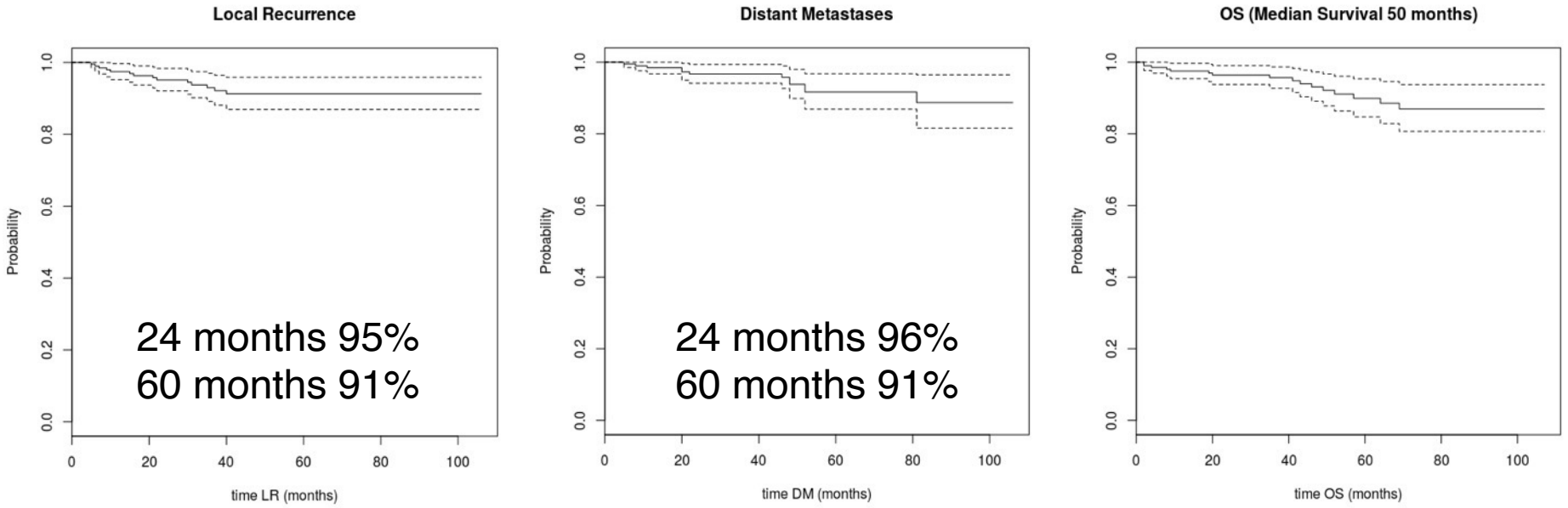
- Radiation retinopathy, radiation optic neuropathy, and radiation-induced macular edema remain devastating sources of vision loss following radiation therapy for globe, and head and neck malignancies.
- Early treatments with laser therapy for radiation-induced macular edema had varying efficacies, but newer treatments with anti-VEGF therapies and steroid-based therapies may have remarkable results on retinal thickness and visual acuity.
- Preventive management with scatter laser and anti-VEGF therapy for radiation-induced macular edema may reduce retinal swelling and improve visual acuity in the long term following radiation therapy.

PREVENTIVE STRATEGY

OF RADIATION MACULOPATHY

TO WHICH PATIENTS SHOULD IT BE OFFERED?

- Gupta A, Muecke JS. Treatment of radiation maculopathy with intravitreal injection of bevacizumab. **Retina. 2008**
- Reichstein D. Current treatments and preventive strategies for radiation retinopathy. **Curr Opin Ophthalmol. 2015**

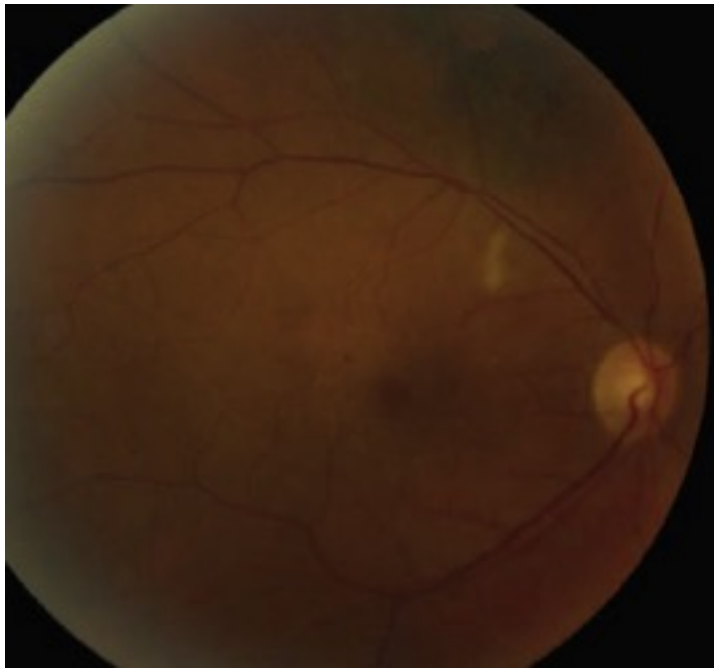


The median follow-up was 41 months

- Luca Tagliaferri, Monica Maria Pagliara, Carlotta Masciocchi, Andrea Scupola, Luigi Azario, Gabriela Grimaldi, Rosa Autorino, Maria Antonietta Gambacorta,Antonio Laricchiuta, Luca Boldrini, Prof. Vincenzo Valentini, Maria Antonietta Blasi. Nomogram for predicting radiation maculopathy in patients treated with Ruthenium-106 plaque brachytherapy for uveal melanoma **J Contemp Brachytherapy 2017**

Maculopathy was recorded using

- **Ophthalmoscopic examination**
- **Optical Coherence Tomography (OCT)**



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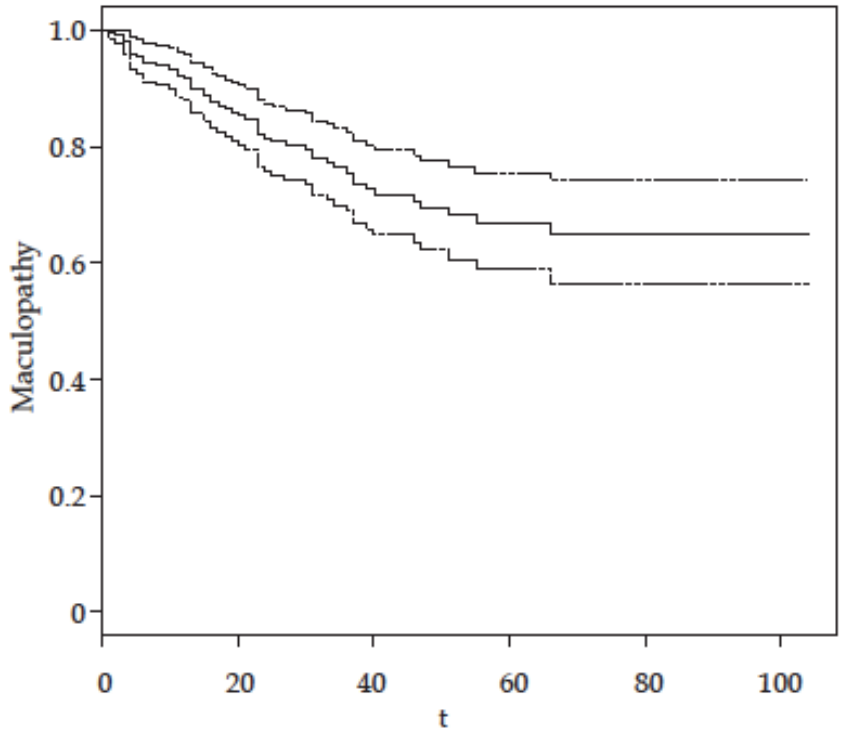

Fig. 2. Kaplan-Meier curve of maculopathy (solid line) with confidence interval (dashed line)

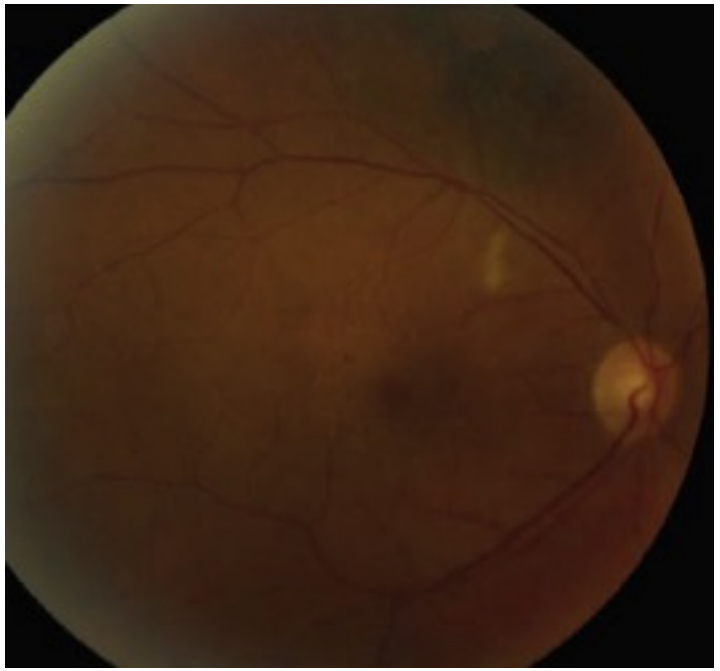

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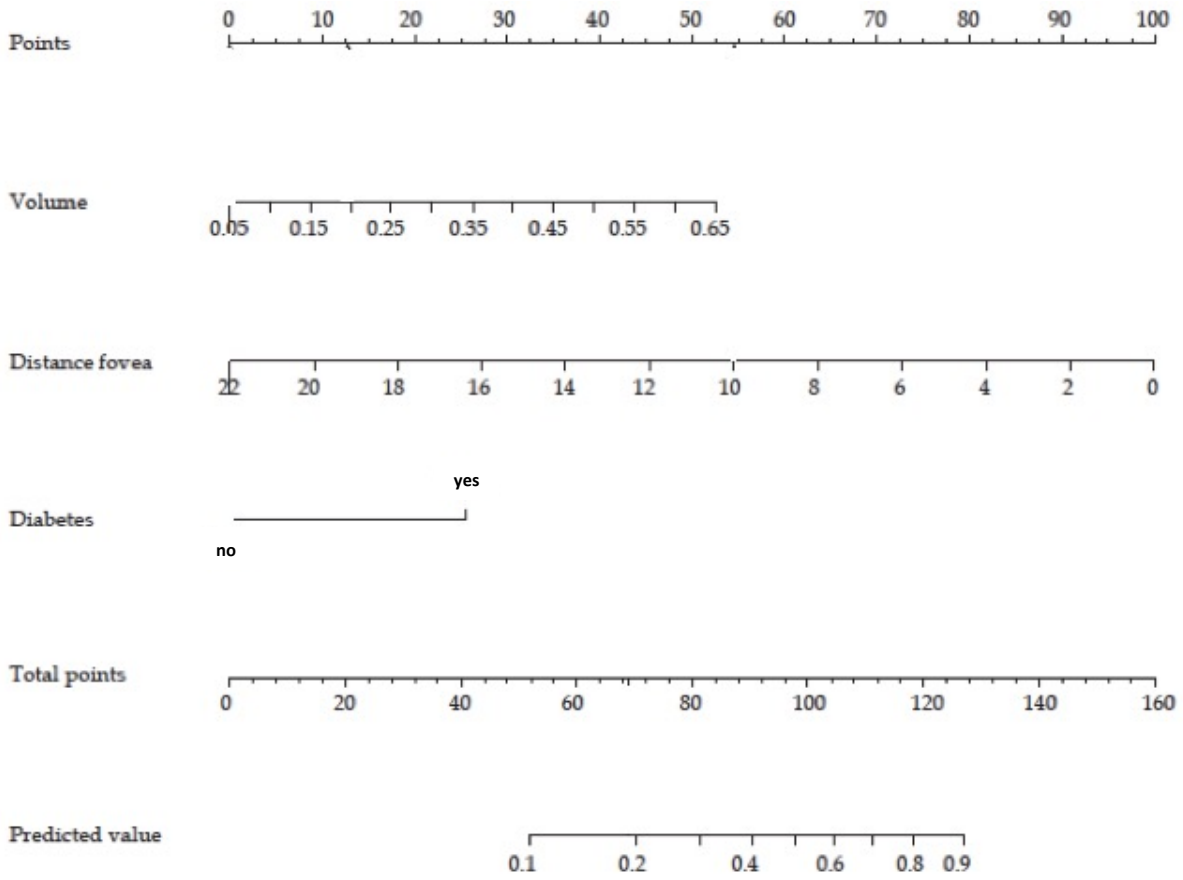
Table 2. Univariate and multivariate analysis for predicting the occurrence of maculopathy at 3 years

Factors	Univariate analysis		Multivariate analysis	
	p-value	Hazard ratio	95% CI	*p*-value
Retinal detachment	0.01*	–	–	0.06
Diabetes	0.02*	2.92	1.38-6.20	< 0.01*
Tumor thickness (mm)	0.03*	–	–	0.53
Distance from fovea (mm)	< 0.01*	0.83	0.76-0.90	< 0.01*
Dose to fovea (Gy)	< 0.01*	–	–	0.80
Dose to optic disk (Gy)	< 0.01*	–	–	0.65
Volume (ml)	0.03*	21.61	1.66-281.14	0.02*
Distance from optic nerve (mm)	< 0.01*	–	–	0.15
Distance from lens (mm)	< 0.01*	–	–	0.86

**Statistical significant: p-value < 0.05*

- Luca Tagliaferri, Monica Maria Pagliara, Carlotta Masciocchi, Andrea Scupola, Luigi Azario, Gabriela Grimaldi, Rosa Autorino, Maria Antonietta Gambacorta,Antonio Laricchiuta, Luca Boldrini, Prof. Vincenzo Valentini, Maria Antonietta Blasi. Nomogram for predicting radiation maculopathy in patients treated with Ruthenium-106 plaque brachytherapy for uveal melanoma **J Contemp Brachytherapy 2017**

to predict maculopathy at 3 years



AUC of 0.75

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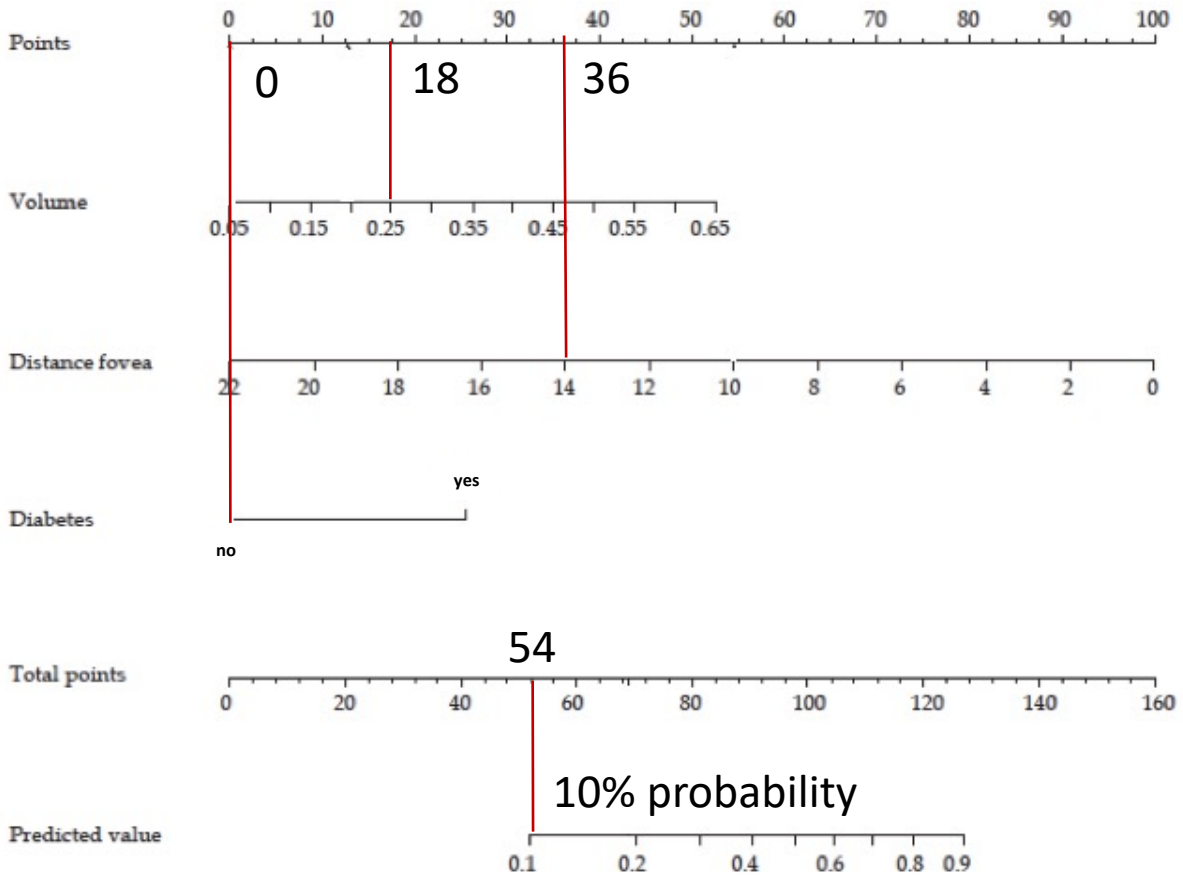
to predict maculopathy at 3 years



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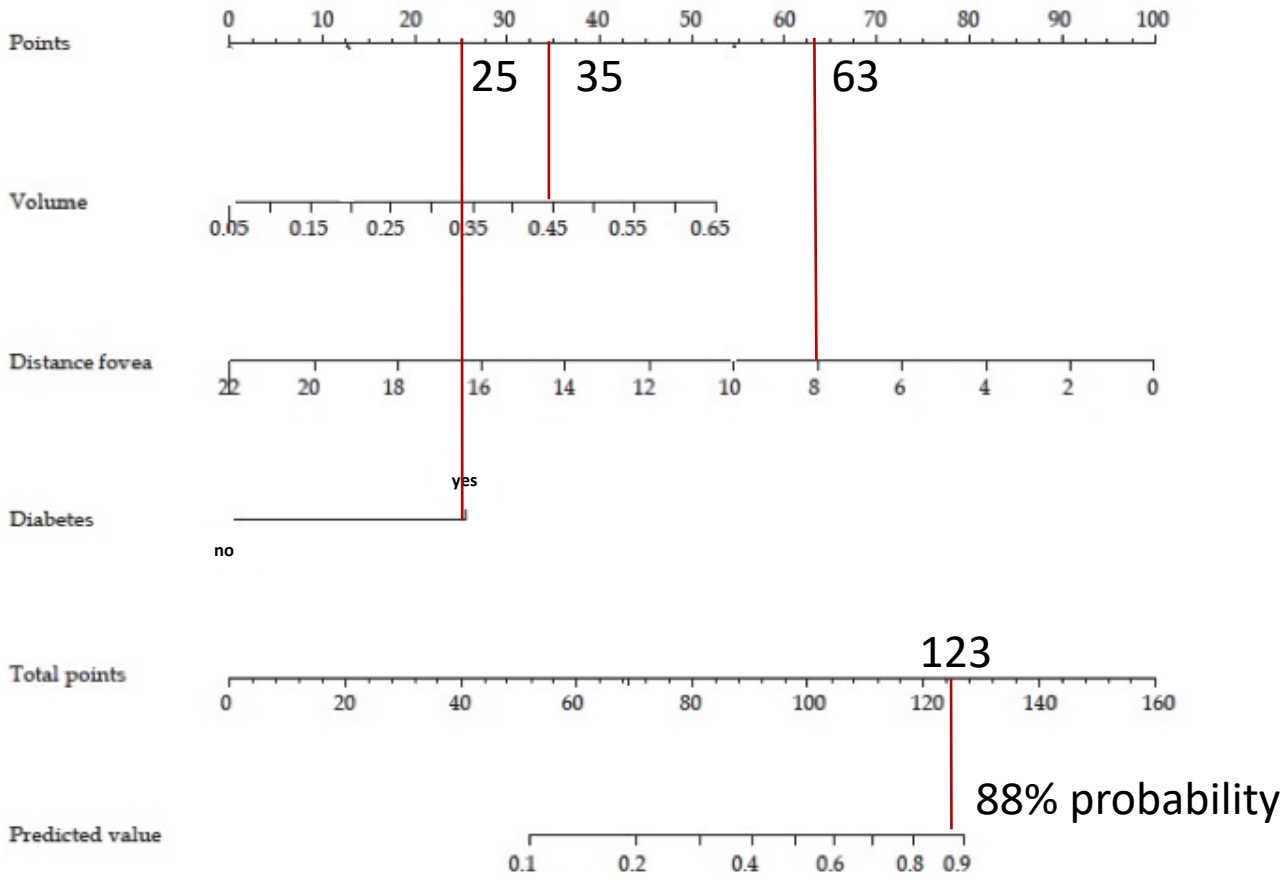

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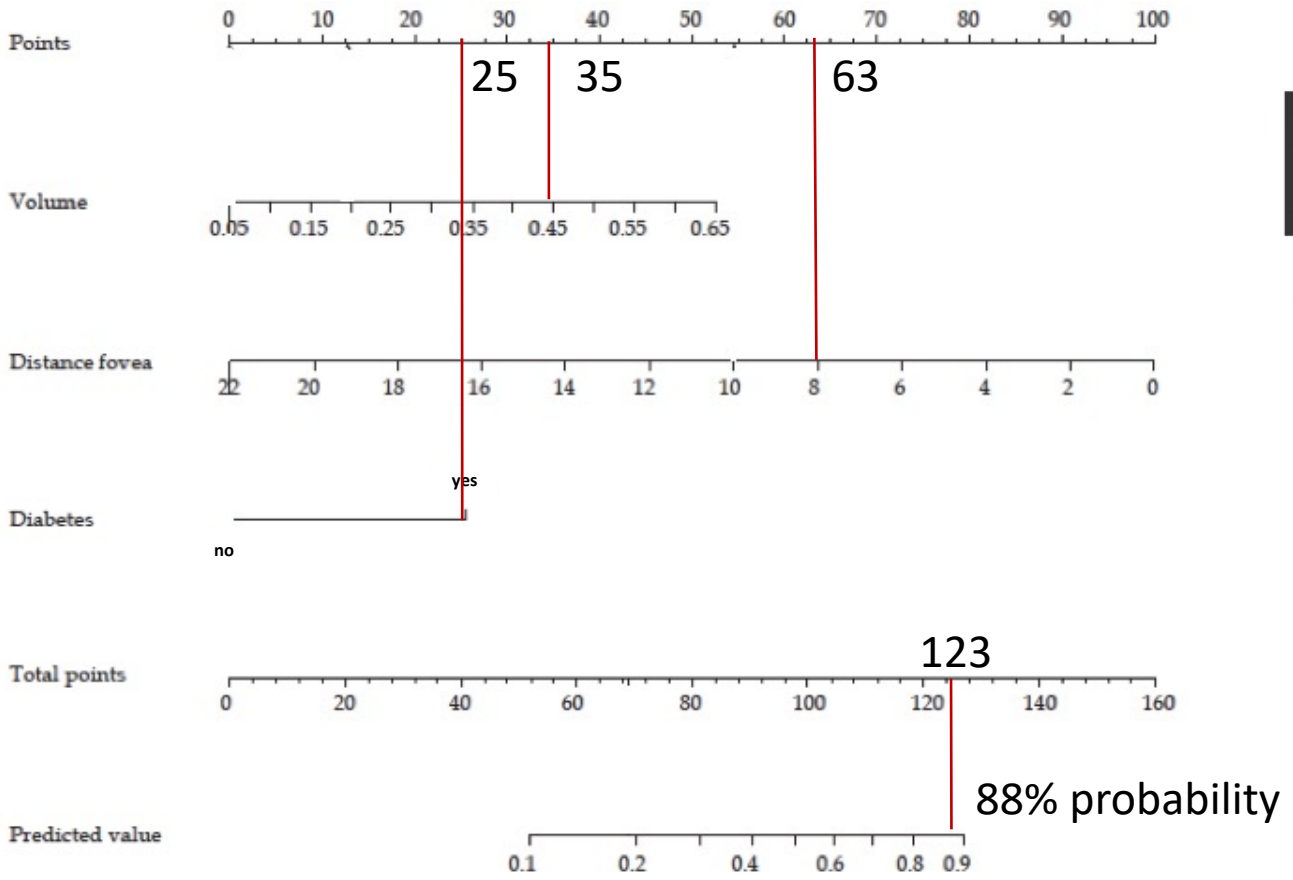

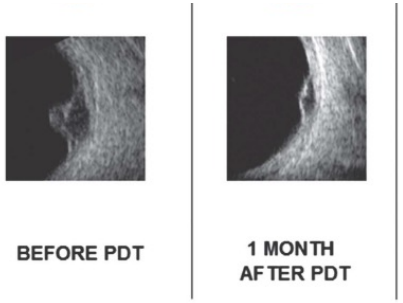

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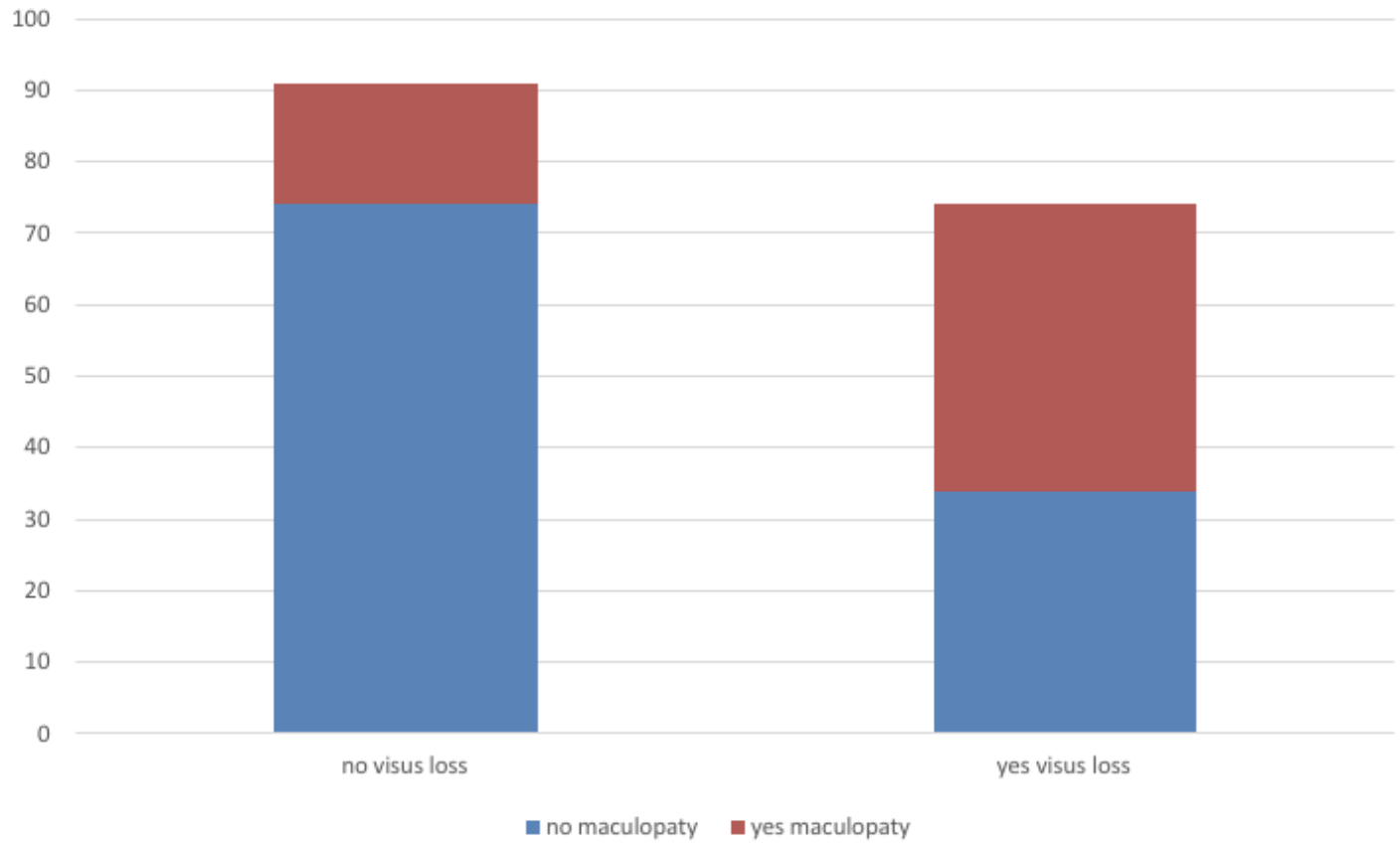
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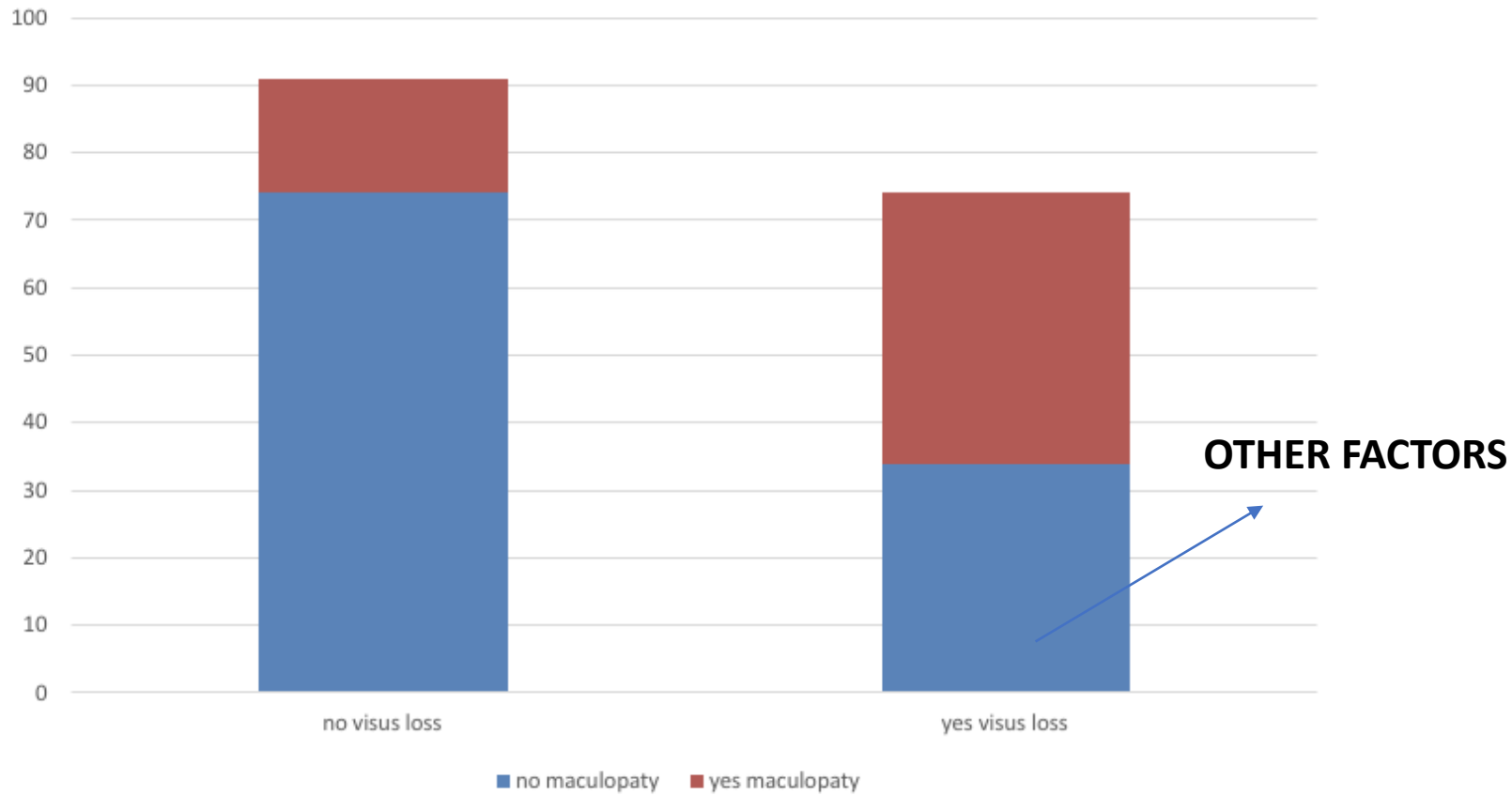
yes maculopaty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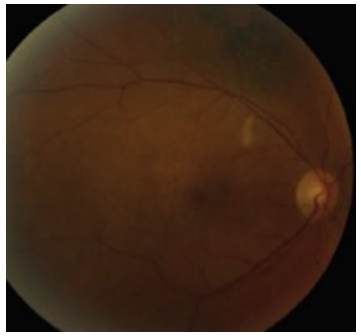
OTHER FACTORS

MACULOPATHY



OTHER FACTORS

?

LOSS OF VISUS

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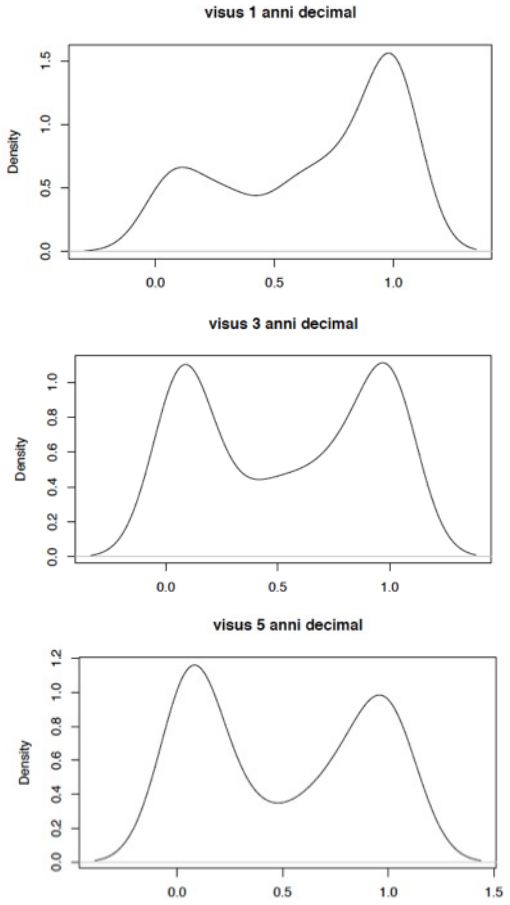
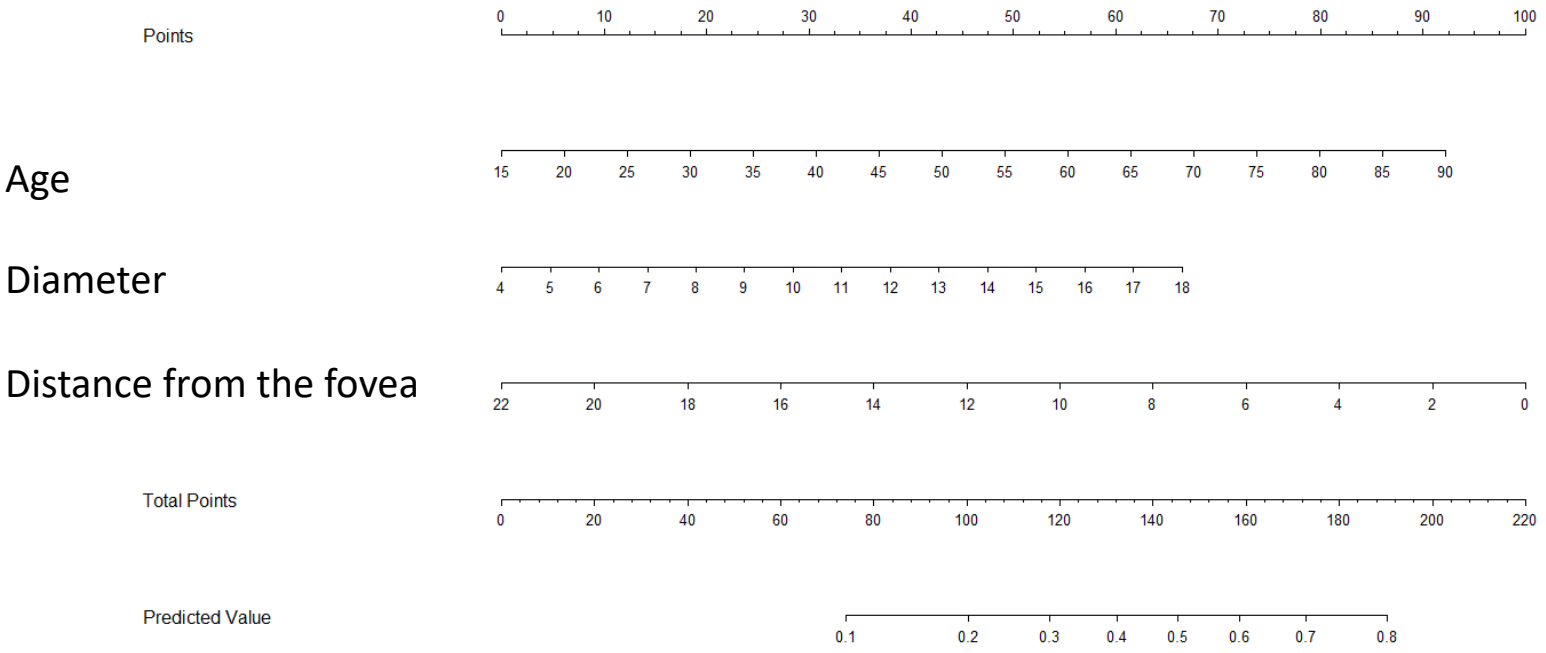


3 YEARS

BEST TIME FOR VISUS LOSS PREDICTIVE MODEL

- AVATAR: Analysis for Visual Acuity Prediction After Eye Interventional Radiotherapy. - Pagliara MM, Tagliaferri L, Lenkowicz J, Azario L, Giattini D, Fionda B, Sammarco MG, Lancellotta V, Gambacorta MA, Blasi MA. In Vivo. 2020



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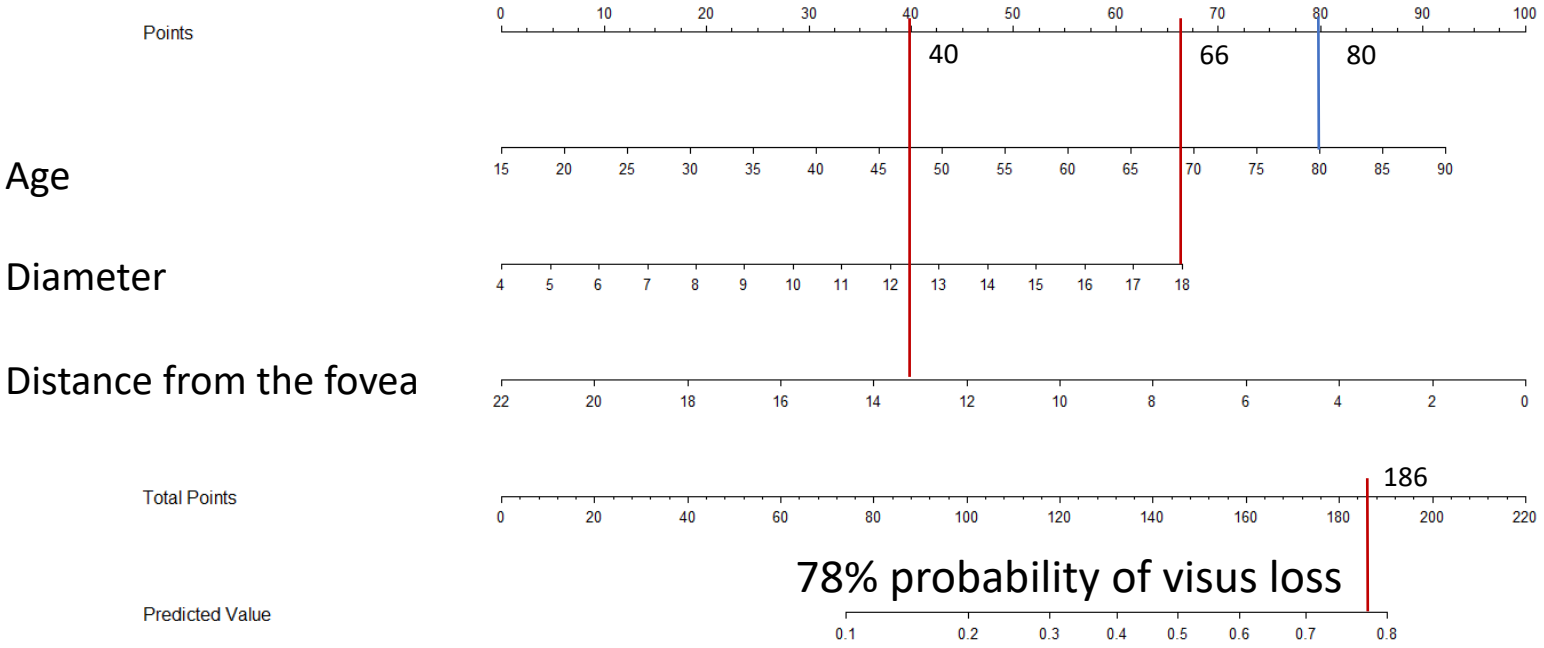

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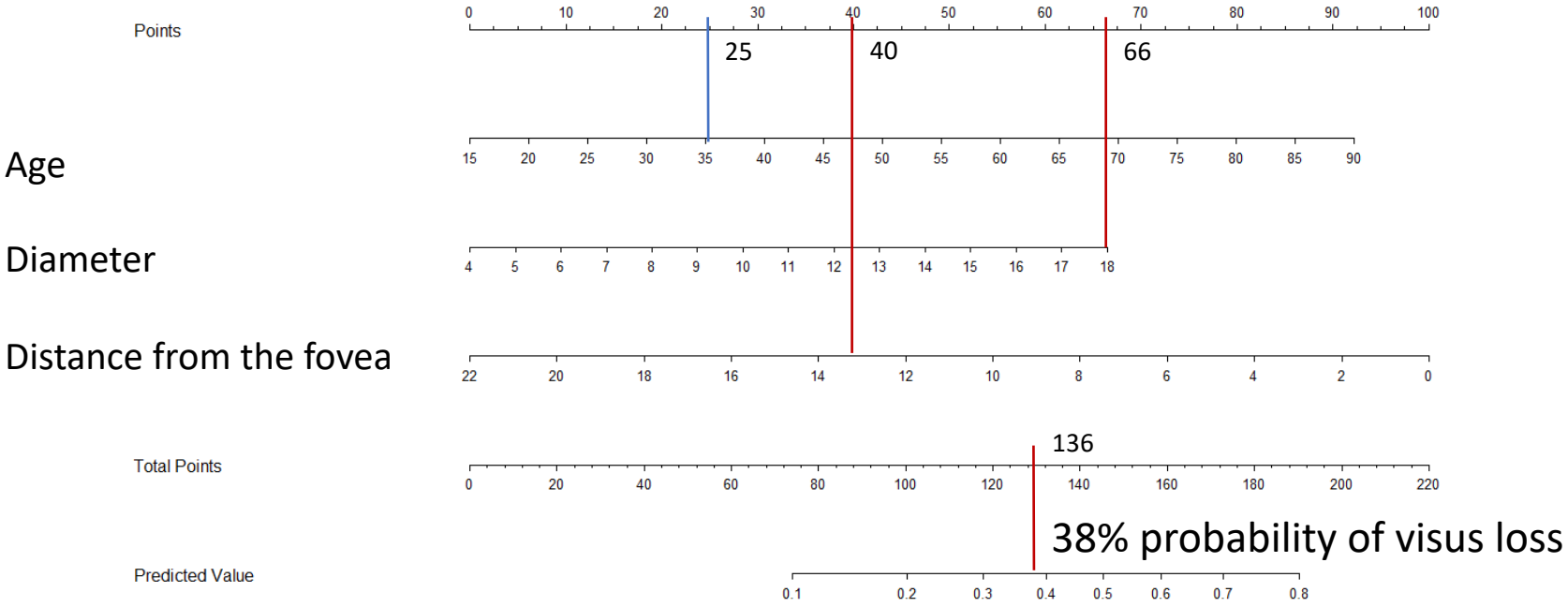

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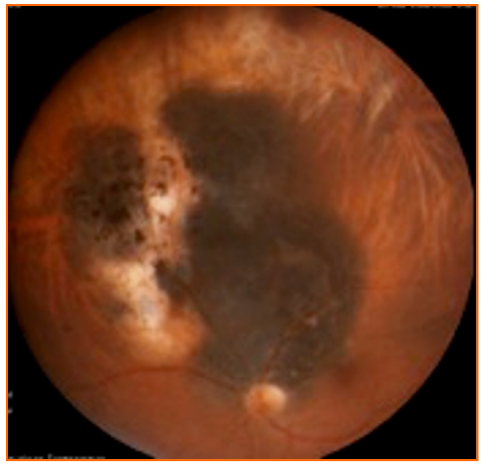
CONCLUSION



EYE
INTERVENTIONAL
RADIOTHERAPY

EXELLENT
LOCAL CONTROL
ORGAN SPARING