Applicazione dell'IA nella valutazione dei biomarkers infiammatori nell'Edema Maculare Diabetico

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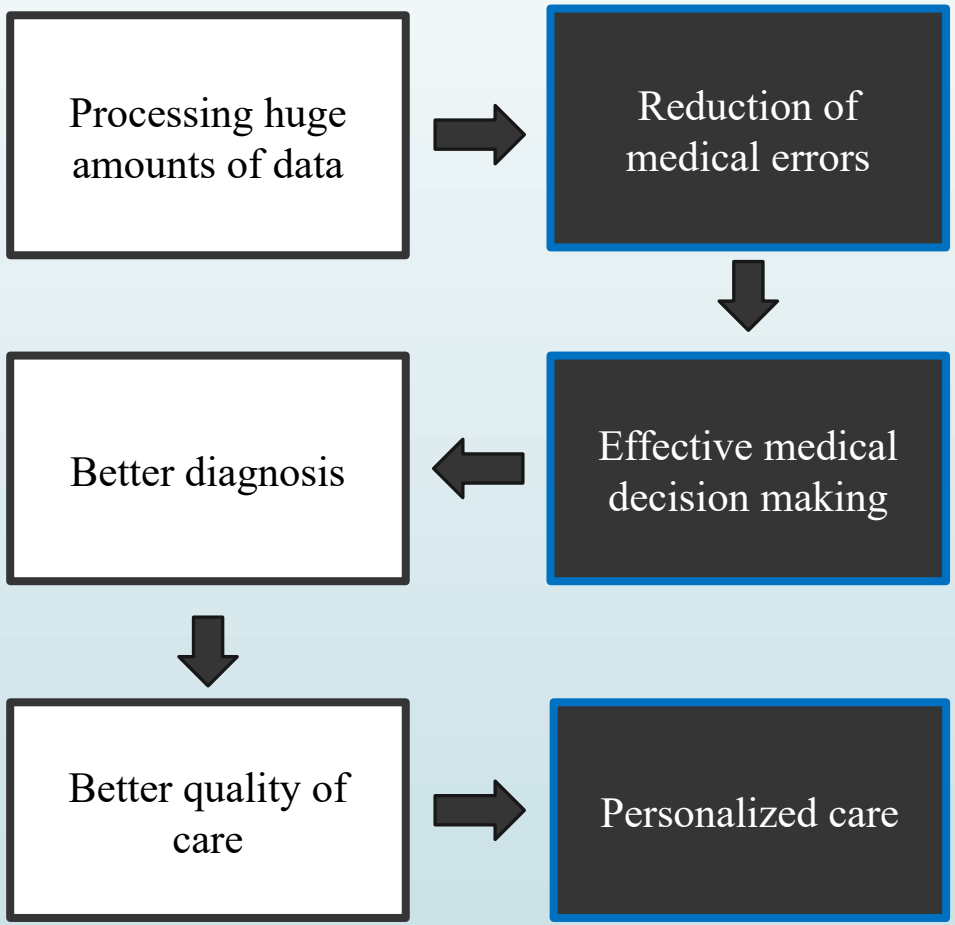
XLIX Congresso Regionale SOSi, 10-12 Aprile 2025, Giardini Naxos

“Artificial intelligence (AI) systems are set to transform the way we think about diagnosing and treating diseases”

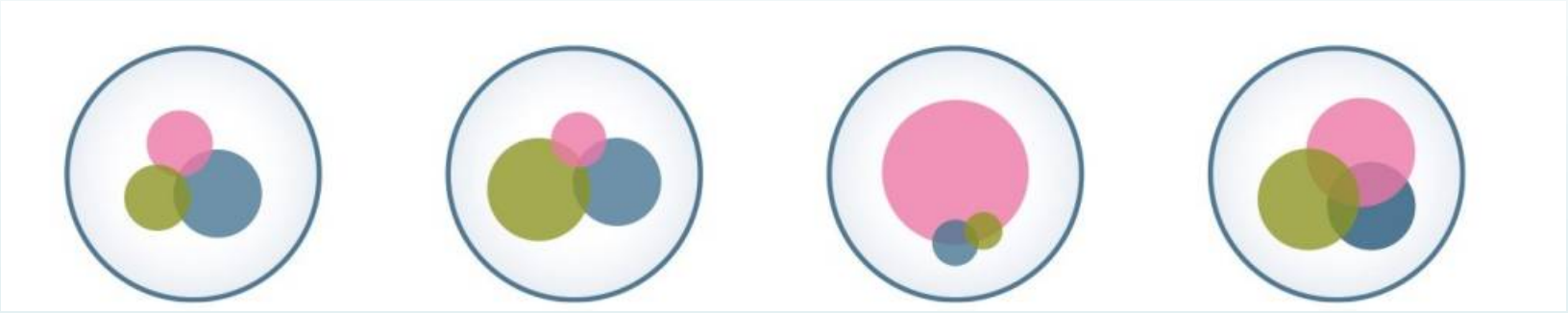
Harpreet Singht Buttar, Frost & Sullivan analyst

AI in medicine: which advantages?



Role of Inflammation

It plays a key role in the pathogenesis of retinal diseases:[1,2]



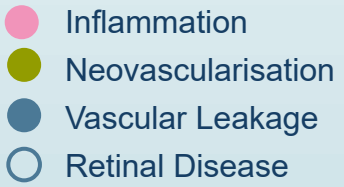
Retinal Vein Occlusion (RVO)[1]

Wet age-related Macular Degeneration (wet AMD)[2]

Uveitis[1]

Diabetic Retinopathy (DR) /Diabetic Macula Edema (DME)[1]

- **In the aqueous humor** of patients with diabetic retinapathy, there is **an increasing of proinflammatory cytocines in addition to VEGFs**.[3]
- **Cytokine concentrations** (except that of VEGF) **correlate significantly** with the severity of DR.[4]



1 Johnson MW. AM J Opthalmol 2009; 147: 11-21. **2** Nowak JZ. Pharmacol Rep 2006; 58: 353-6 3. **3** Lee WJ et al. Br J Ophthalmol 2012; 96:1426–30. **4** Dong N et al. Mol Vis 2013; 19:1734–46. VEGF = vascular endothelial growth factor

Aqueous Humor Cytokines in Diabetic Retinopathy

In a study comparing the changes in concentrations of 27 aqueous humor cytokines between nondiabetic controls and diabetic patients with various severities of retinopathy, inflammatory mediators, but not VEGF, were found to be correlated with DR severity.

Relationship between the concentrations of the assayed cytokines and the severity of DR							
Level[a]	N	VEGF (SD)	IL-1β (SD)	IL-6 (SD)	IL-8 (SD)	MCP-1 (SD)	IP-10 (SD)
10	28	967.0 (425.1)	10.0 (12.4)	32.1 (33.8)	22.8 (22.1)	252.5 (227.6)	2.1 (1.73)
20	23	952.8 (355.9)	11.0 (18.4)	33.5 (37.1)	20.6 (25.5)	303.6 (159.32)	2.5 (2.7)
35	26	956.4 (378.7)	9.2 (14.4)	33.1 (40.6)	22.7 (31.1)	339.5 (244.8)	5.6 (4.0)
43	18	1084.7 (349.9)	10.7 (16.4)	33.2 (43.3)	24.4 (33.1)	468.8 (273.9)	5.5 (3.9)
47	13	1172.6 (423.1)	18.8 (15.3)	56.6 (51.4)	29.2 (33.7)	645.2 (318.7)	9.5 (12.1)
53	8	1177.3 (534.5)	22.7 (17.1)	106.7 (52.7)	49.4 (41.5)	921.2 (391.1)	22.3 (16.7)
65	7	1142.7 (573.3)	23.7 (29.0)	116.8 (60.4)	51.0 (22.8)	1215.1 (435.9)	31.3 (24.4)
75	8	1051.4 (296.6)	27.6 (36.0)	147.0 (97.1)	75.7 (58.9)	1286.6 (383.4)	34.3 (20.1)
81	5	1165.4 (326.8)	45.8 (33.1)	188.6 (106.6)	74.4 (59.3)	1630.8 (601.2)	29.2 (18.6)
p-value		0.733	0.003	<0.001	0.001	<0.001	<0.001

Aqueous humor levels of VEGF **were not significantly** correlated with DR severity

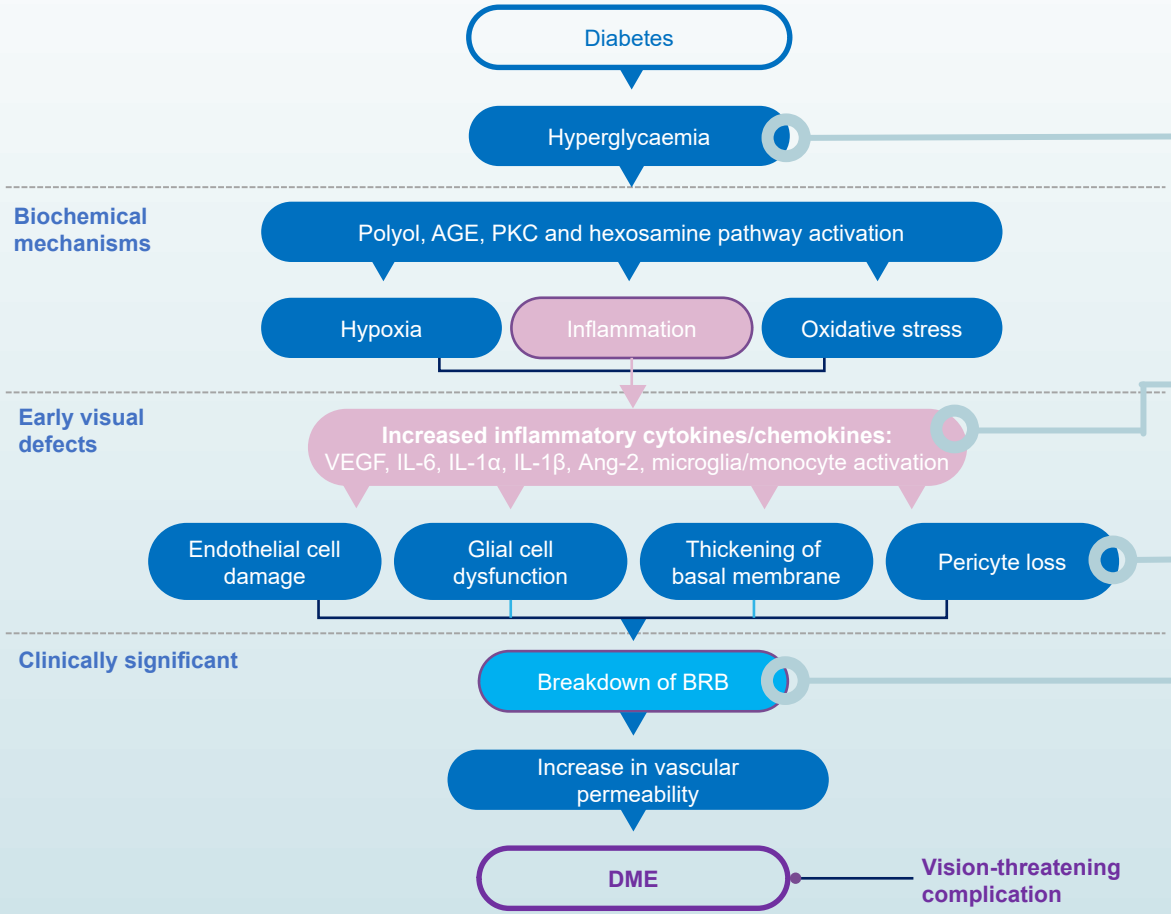
Aqueous humor levels of IL-1β, IL-6, IL-8, MCP-1 and IP-10 **increased significantly** with DR severity

[a] ETDRS retinopathy severity

ETDRS = Early Treatment Diabetic Retinopathy Study; IL = interleukin; IP = interferon-induced protein; MCP = monocyte chemoattractant protein; VEGF = vascular endothelial growth factor

Dong N, et al. Molecular Vision. 2013;19:1734-1746.

Inflammation contributes to the breakdown of BRB and onset of DME[1–4]



Hyperglycaemia induces overactivation of biochemical pathways, which lead to hypoxia, inflammation and oxidative stress.[1,2]

These stress conditions increase production of inflammatory cytokines/chemokines.[3]

Example: pericyte loss causes damage such as hypoperfusion, neovascularisation and neurodegeneration.[4]

Leading to the breakdown of the BRB and increased vascular permeability.[3]

Figure adapted from Das A et al. 2015[5], Urias EA et al. 2017[3] and Ansari P et al. 2022[4]

AGE, advanced glycation end product; Ang, angiopoietin; BRB, blood–retinal barrier; DME, diabetic macular oedema; IL, interleukin; PKC, protein kinase C; VEGF, vascular endothelial growth factor.

1. Bahrami B, et al. *Diabetologia.* 2016;59(8):1594–608; 2. Wu MY, et al. *Oxid Med Cell Longev.* 2018;2018:3420187; 3. Urias EA, et al. *Vision Res.* 2017;139:221–7; 4. Ansari P, et al. *Diabetology.* 2022;3(1):159–75; 5. Das A, et al. *Ophthalmology.* 2015;122(7):1375–94.

Inflammatory Biomarkes

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ELSEVIER

Review article

Multimodal imaging in diabetic retinopathy and macular edema: An update about biomarkers

Mariacristina Parravano [a], Gilda Cennamo [b], Luca Di Antonio [c], Maria Oliva Grassi [d], Marco Lupidi [e], Marco Rispoli [f], Maria Cristina Savastano [g,h], Daniele Veritti [i], Stela Vujosevic [j,k,*]

- **HRF:** hyperreflective foci
- **ELM/EZ INTERRUPTION**
- **SUBFOVEAL NEURORETINAL DETACHMENT**
- **DRIL:** disorganization of retinal inner layers

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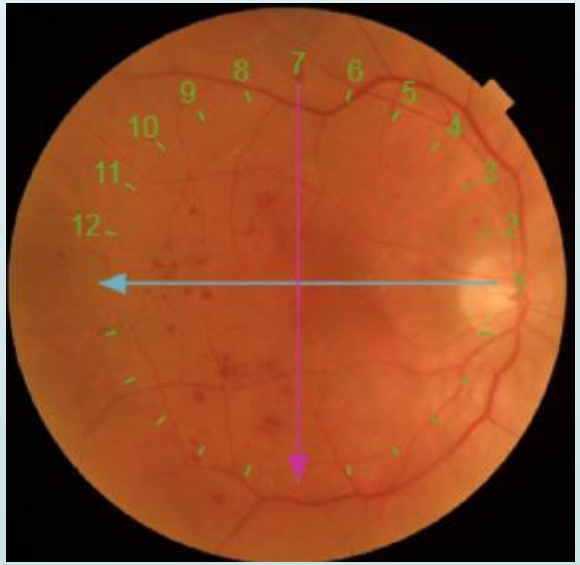
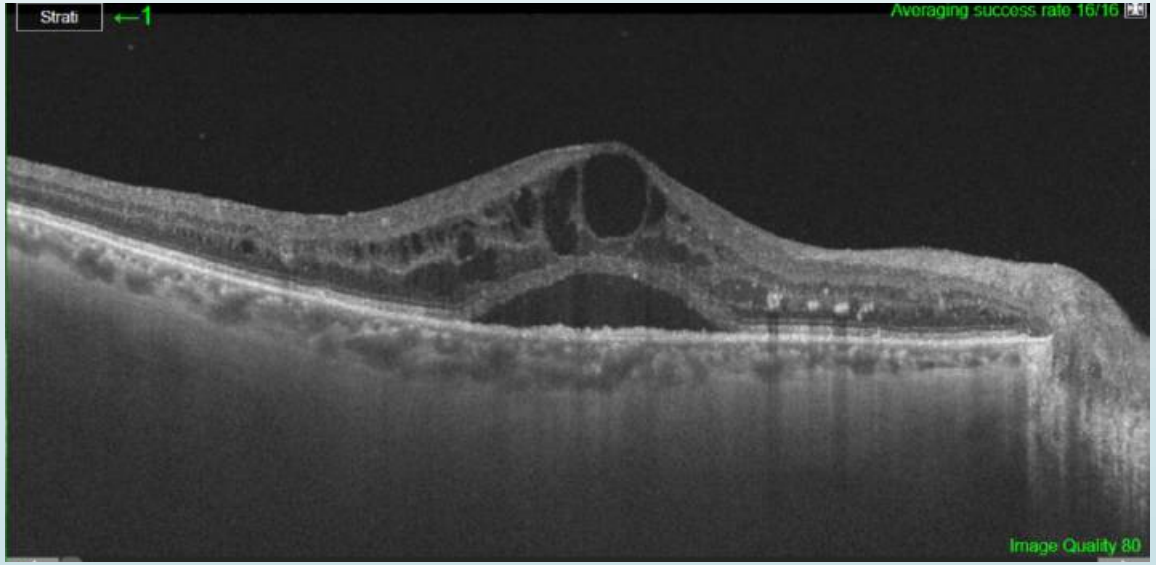
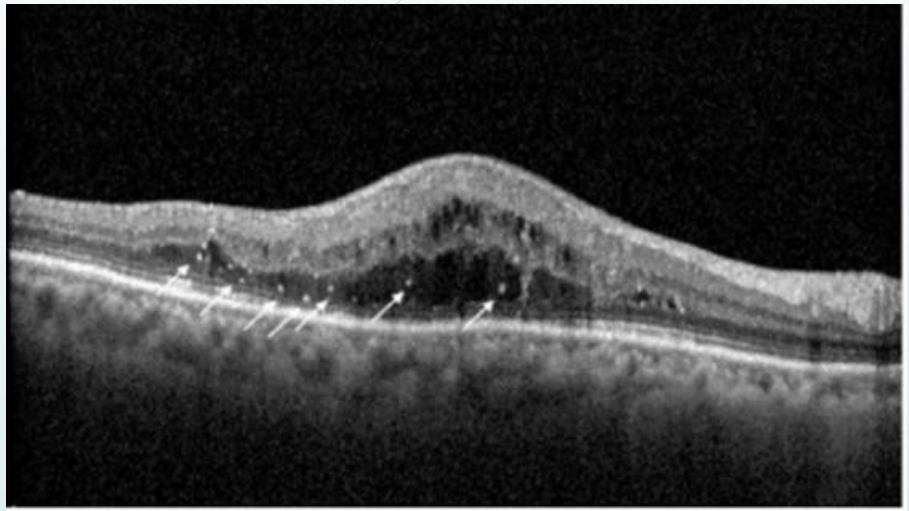




J.K. Sun et al, Diabetes 2015
S. Radwan et al, JAMA Ophth 2015
S.Vujosevic et al. Acta Ophtalmol 2017
M. Parravano et al. Acta Diabetol 2020
M.Parravano et al. Surv Ophthalmol 2024

Hyper-reflective foci



d: HRF (white arrows)
Note the well circumscribed dots that are </=30µm in diameter with reflectivity similar to the RNFL and without back shadowing

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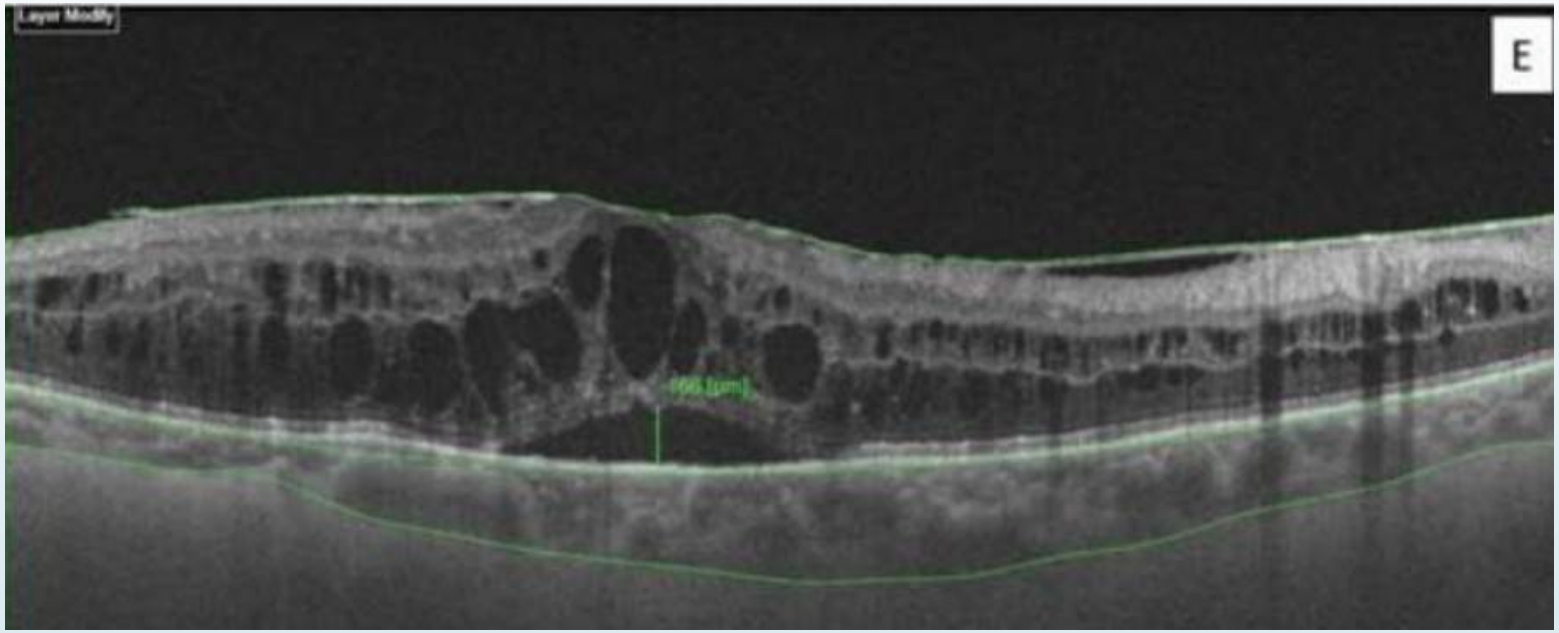
Well-circumscribed spots, distinguishable from hard exudates by the following characteristics:

- Moderate reflectivity
- Absence of posterior shadows
- Small diameter (≤ 30 µm)
- Well-circumscribed round shape
- Not related to retinal vessels

The inflammatory nature of HRFs is supported by several studies.

- Kokona et al.,2017: HRFs observed on OCT correspond to macrophages in histology and fluorescence-activated flow cytometry.
- Lee et al., 2018: Proteomic analysis showed that the presence of HFs strongly correlates with increased levels of CD14, a cytokine released by microglia and macrophages, further supporting the idea that HFs are activated microglia.

Subfoveal neuroretinal detachment



It is a serous detachment of the neuroepithelium due to the formation of subretinal fluid due to leakage from the choriocapillaris:

- Associated with high levels of IL6 and IL8
- Associated with high presence of HRF

Efficacy of dexamethasone implant on diabetic macular edema

Anatomic Response to Intravitreal Dexamethasone Implant and Baseline Aqueous Humor Cytokine Levels in Diabetic Macular Edema

Marc Figueras-Roca,[1,2] Anna Sala-
Socorro Alforja,[1,2] Cristina Esquir
[1]Institut Clínic d'Oftalmologia (ICOF), Hosp
[2]August Pi i Sunyer Biomedical Research In
[3]Respiratory Department, Hospital Universi

Original Article

Effect of dexamethasone implant on intraocular cytokines in diabetic macular edema

Gupta, Tessy Xavier[1], Natasha Radhakrishnan, Krishnakumar N Menon[1], Rehna Rasheed, Greeshma C Ravindran[2]

luate intraocular cytokines (IC) before and after dexamethasone
secondary aim was to study the early and late effects of single
ds: This before and after comparative study was conducted at the
tre for Nanosciences at a quaternary referral center in Kerala, India,
. Patients underwent complete ophthalmological examination and
ethasone implant. Levels of cytokines at baseline and repeat sample
(21 patients) were divided into two groups depending on time from
uded patients with <3 months between the two samples – 12 (44.4%).
nths between the two samples –15 (55.6%). Best corrected visual
ickness (CMT) improved significantly post-dexamethasone in
(IL)-4, IL-6, IL-10, vascular endothelial growth factor (VEGF), IL-1β,
(IP-10), monocyte chemoattractant protein-1 (MCP-1), and IL-2
cytokines increased post-dexamethasone in group 2, except IL-10.
to half in group 1 (*P*-value 0.814) and it tripled in group 2 (*P*-value
second samples was not different in either group. **Conclusion:** Our
nore on IC than VEGF in DME. This is significant in the first 3 months
nths. Our study also suggests that repeat injection of DEX in DME
eterioration of visual acuity (VA) and worsening of CMT.

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DOI: 10.4103/ijo.IJO_1280_22
Quick Response Code:

> J Ophthalmol. 2021 Mar 24:2021:6639418. doi: 10.1155/2021/6639418. eCollection 2021.

Optical Coherence Tomography Predictors of Favorable Functional Response in Naïve Diabetic Macular Edema Eyes Treated with Dexamethasone Implants as a First-Line Agent

Alessandro Meduri [1], Giovanni William Oliverio [1], Luigi Trombetta [1], Marta Giordano [1], Leandro Inferrera [1], Costantino John Trombetta [1]

> Diagnostics (Basel). 2020 Jun 17;10(6):413. doi: 10.3390/diagnostics10060413.

The Application of Structural Retinal Biomarkers to Evaluate the Effect of Intravitreal Ranibizumab and Dexamethasone Intravitreal Implant on Treatment of Diabetic Macular Edema

Ida Ceravolo [1], Giovanni William Oliverio [1], Angela Alibrandi [1], Ahsan Bhatti [2], Luigi Trombetta [1]

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Clinical and optical coherence tomography biomarkers as prognostic factors in **dexamethasone** intravitreal implant for diabetic macular edema.

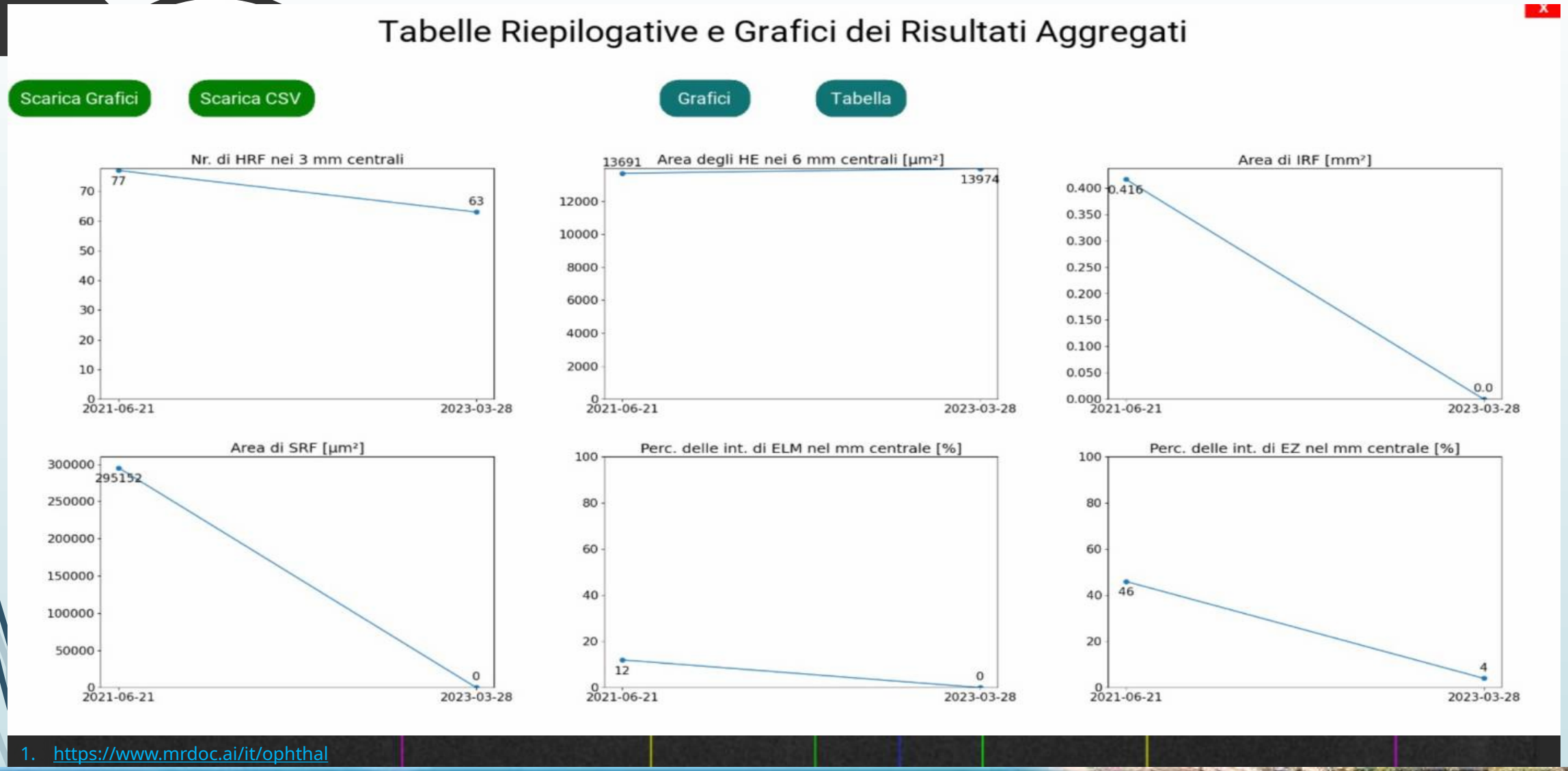
Oliverio GW, Meduri A, Brancati VU, Ingrande I, De Luca L, Raimondo ED, Minutoli L, Aragona E, Aragona P.

Eur J Ophthalmol. 2024 Nov;34(6):1810-1818. doi: 10.1177/11206721241235242. Epub 2024 Feb 21.

PMID: 38384119

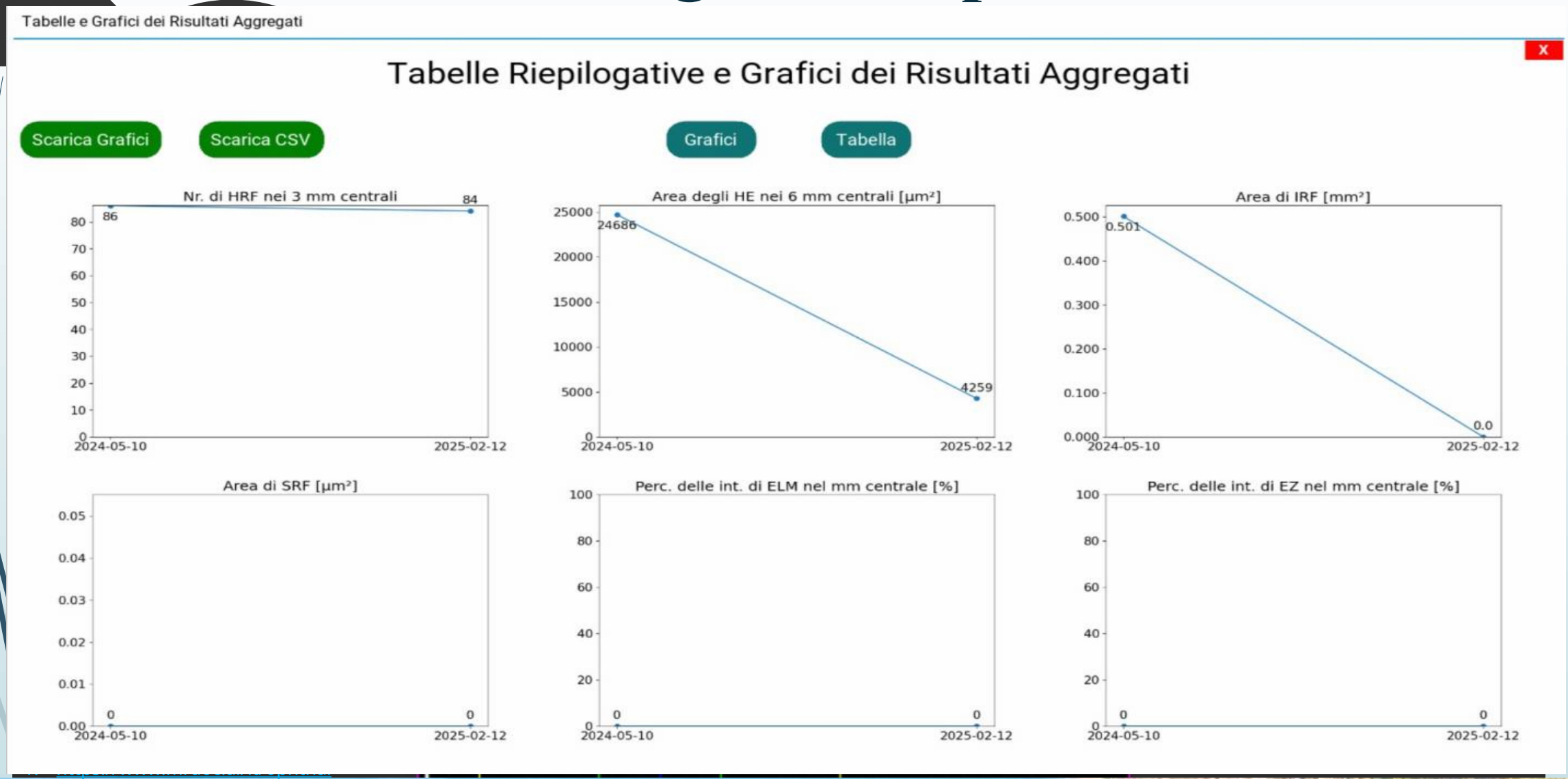
PURPOSE: Aim of the study was to evaluate the efficacy of **dexamethasone** (DEX) 0.7 mg intravitreal

AI in retinal diagnosis: Ophtal, Mr.Doc[1]



1. https://www.mrdoc.ai/it/ophthal

AI in retinal diagnosis: Ophtal, Mr.Doc[1]



UTILITY OF THIS ALGORITHM

- It provides reliable and reproducible assessment of the most relevant OCT biomarkers in DME and a clearer view of the different retinal layers.
- It can enable clinicians to routinely identify and quantify various parameters (IRF, SRF, ELM-EZ integrity, HRF quantification), providing an objective way to diagnose and follow up on DME patients.
- It can help the clinician in choosing the correct drug to administer to the patient with DME as intravitreal therapy.

THANKS FOR YOUR ATTENTION