CRITÈRES PRÉDICTIFS DU TRAITEMENT DE L'OMD

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Liens d'intérêt

- Allergan
- Bayer
- Novartis

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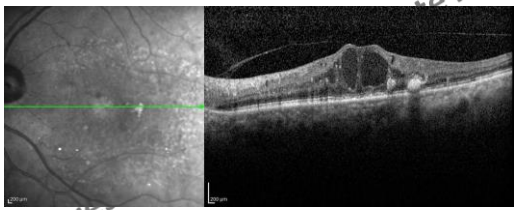
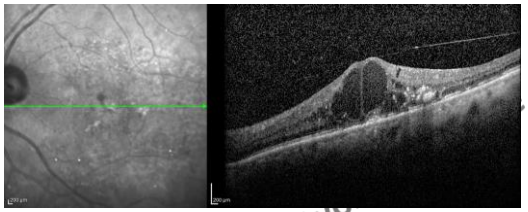
Prédire la réponse au traitement

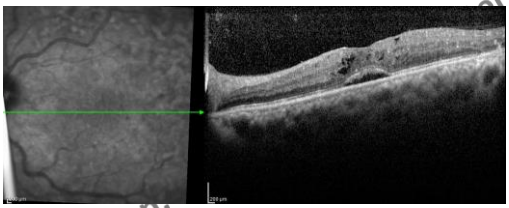
- F 58 ans, Hba1c 5.9%, RDP



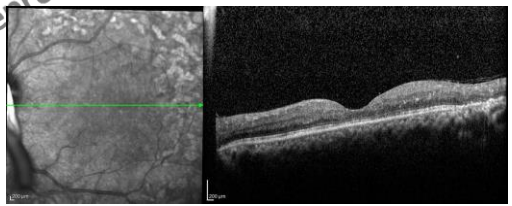
16 anti-VEGF, 1 DEX implant



- H 54 ans, Hba1c 6.9%, RDP

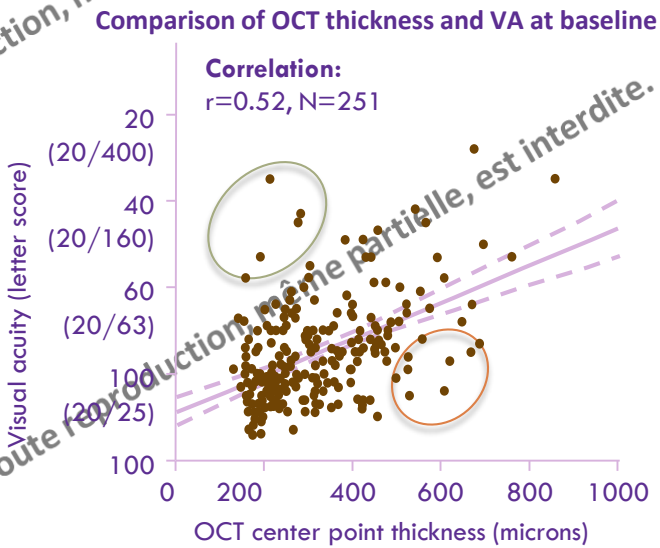


5 anti-VEGF IVI



Définir la réponse

- Anatomique
  - Diminution de l'EMC d'au moins 10 %
- Fonctionnelle
  - Gain AV > 5 lettres



Adapted from Diabetic Retinopathy Clinical Research Network, Browning DJ, *et al. Ophthalmology* 2007;114:525–36.

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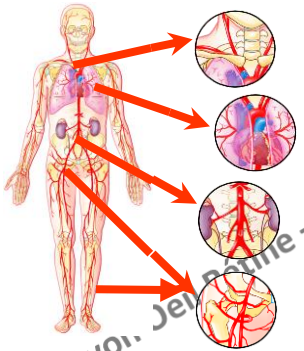
Critères prédictifs de la réponse aux injections



- Études randomisées
- Études de vraie vie

Acuité visuelle initiale

- AV initiale basse corrélée à
  - AV finale plus faible
  - Moins de patients ayant MAVC finale ≥ 20/40
  - Malgré un gain plus important

L'AV initiale conditionne l'AV finale

Dans les étude randomisées

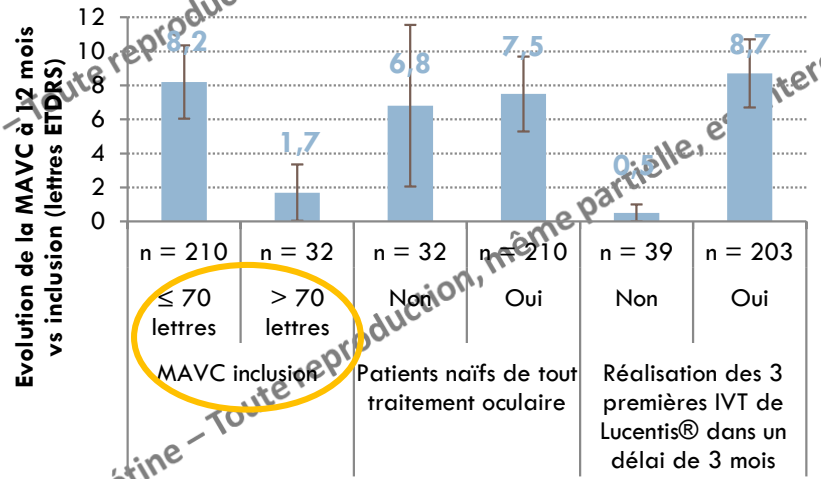
Aflibercept, Bevacizumab, or Ranibizumab for Diabetic Macular Edema

Two-Year Results from a Comparative Effectiveness Randomized Clinical Trial

Visual Acuity	Observed Data		
	Aflibercept	*Bevacizumab*	*Ranibizumab*
Baseline visual acuity 20/50 or worse (letter score, <69)			
No. of patients	98	92	94
Baseline			
Mean ± SD	55.8±11.1	56.9±10.5	56.1±10.1
~Snellen equivalent	20/80	20/80	20/80
1 year (in 2-yr cohort)			
Mean ± SD	75.4±10.4	69.6±12.0	70.8±12.0
~Snellen equivalent	20/32	20/40	20/40
Mean change ±SD	19.4±11.1	12.6±11.8	14.7±10.2
2 year			
Mean ± SD	74.3±13.3	69.8±15.7	71.9±14.6
~Snellen equivalent	20/32	20/40	20/40
Baseline visual acuity 20/32–20/40 (letter score, 78–69)			
No. of patients	103	93	97
Baseline			
Mean ± SD	73.5±2.6	73.0±2.9	73.4±2.7
~Snellen equivalent	20/32	20/40	20/40
1 year (in 2-yr cohort)			
Mean ± SD	81.3±8.3	79.8±10.5	81.8±6.8
~Snellen equivalent	20/25	20/25	20/25
Mean change±SD	7.9±7.7	7.3±7.3	8.4±6.8
2 year			
Mean ± SD	81.2±8.3	79.3±11.4	82.0±6.8
~Snellen equivalent	20/25	20/25	20/25

BOREAL Diabète

- L'analyse en sous-groupes a montré que les 2 facteurs corrélés avec un meilleur gain d'AV étaient :
- l'AV initiale (< 70 lettres)
- la réalisation de 3 injections initiales



Barres : intervalle de confiance à 95%

D'après P. Massin, SFO 2017

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Treatment for Central-involved DME in eyes with Very Good Visual Acuity

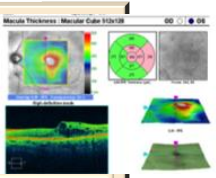
DRCR.net

National Eye Institute
NATIONAL INSTITUTES OF HEALTH

Randomized, multi-center clinical trial

At least one eye meeting *all* of the following criteria:

- **Central-involved DME on OCT (Cirrus/Spectralis only)***
- **VA letter score 20/25 or better*** **AV >8/10e**
- **No prior treatment for DME**



Prompt anti-VEGF	Prompt laser + deferred anti-VEGF	Observation + deferred anti-VEGF

Primary outcome: Proportion of eyes that have lost ≥5 letters of VA at 2 years

***Confirmed at 2 visits (screening and randomization 1-28 days apart)**

Facteurs généraux

- Sexe masculin
  - READ-2: 59% of females in the poor outcome group vs 35% in the better outcome group (p=0.03)
  - RISE/RIDE: Male gender associated with a final BCVA ≥ 20/40 (p<0.005)
- Âge jeune
  - RESTORE: older age associated with poor BCVA at 36 month
  - RISE/RIDE: young age correlate with VA gain ≥ 15 letters (p=0.02), also in the laser group
  - DRCR.net protocol I: younger age strongly associated with VA improvement at 1 year (p<0.001), +2.2 letters for every 10 years
- Durée de l'OM et durée du diabète
  - RISE / RIDE: a shorter duration correlated with VA gain ≥ 15 letters (p=0.03)
  - DRCR.net protocole I: duration <15 years having better visual acuity gains (p<0.001)

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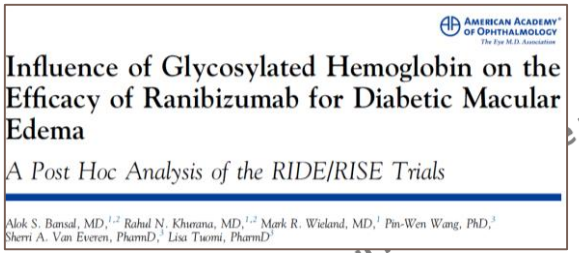
Taux d'hémoglobine glyquée



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The Eye M.D. Association

Influence of Glycosylated Hemoglobin on the Efficacy of Ranibizumab for Diabetic Macular Edema

A Post Hoc Analysis of the RIDE/RISE Trials

Alok S. Bansal, MD,[1,2] Rahul N. Khurana, MD,[1,2] Mark R. Wieland, MD,[1] Pin-Wen Wang, PhD,[3] Sherri A. Van Everen, PharmD,[3] Lisa Tuomi, PharmD[3]

Table 3. Influence of Change of Glycosylated Hemoglobin on Outcomes: Baseline Characteristics and Summary of Results

Characteristic or Outcome	HbA1c Improved* (n = 93)	HbA1c Stable* (n = 139)	HbA1c Worsened* (n = 139)	P Value
Baseline characteristics				
HbA1c, %	8.5 (1.5)	7.3 (1.2)	7.4 (1.2)	–
Age, yrs	63 (8.6)	63 (10.4)	61 (10.0)	–
Male, n (%)	51 (55)	92 (66)	76 (55)	–
Duration of diabetes, yrs	16 (11.1)	16 (9.8)	15 (8.7)	0.41
BCVA, ETDRS letters	55 (11.9)	58 (10.4)	57 (13.2)	0.30
approximate Snellen equivalent	20/80	20/80	20/80	
CFT, µm	457 (144.6)	489 (175.7)	480 (161.8)	0.34
Median DR severity score†	47‡	47‡	47‡	0.17
Vision outcomes at month 36				
Change in BCVA from baseline, ETDRS letters	+12 (15.9)	+13 (13.1)	+15 (13.4)	0.23
BCVA, ETDRS letters	67 (14.9)	70 (13.3)	71 (15.1)	0.07
approximate Snellen equivalent	20/50	20/40	20/40	
Patients gaining ≥15 letters from baseline, n (%)	41 (44)	66 (47)	70 (50)	0.64
Patients with Snellen ≥20/40, n (%)	51 (55)	90 (65)	96 (69)	0.08
Anatomic outcomes at month 36				
Change in CFT from baseline, µm	−248 (176.8)	−295 (200.1)	−304 (178.3)	0.06
Change in CFT from baseline, µm, adjusted LS mean (SE)§	−267 (11.8)	−285 (9.7)	−301 (9.6)	0.08
CFT, µm	209 (126.4)	193 (111.0)	176 (99.4)	0.08
Patients with CFT ≤250 µm, n (%)	75 (81)	115 (83)	127 (91)	0.04
DR severity score at month 36†				
Median DR severity score	35‡	35‡	35‡	0.86
Patients with ≥2-step improvement, n (%)	33 (38)	58 (44)	64 (50)	0.21

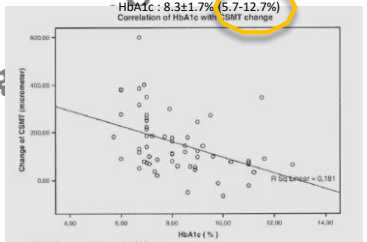
- DRCR.net protocole I
  - Baseline HbA1c did not affect outcomes of treatment, with those with levels <7.5 and >7.5% having similar gains.

Corrélation HbA1c et réponse au traitement dans la vraie vie

- 2 études rétrospectives

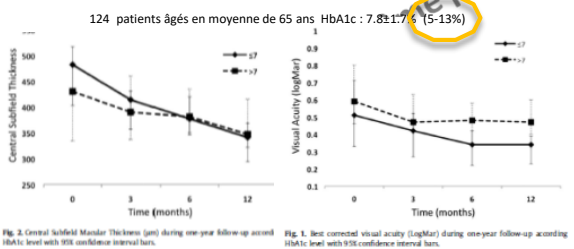
Changement d'épaisseur maculaire
et gain d'AV plus importants dans groupe
avec HbA1c < 7%

Changement d'épaisseur maculaire
inversement corrélé à l'HbA1c



Ozturk BT et al. *J Diabetes Complications* 2011;25:298-302

Niveau d'HbA1c n'influence pas le nb moyen d'IVT



Matsuda S et al. *J Diabetes Complications* 2014;28:166-70.

La réponse initiale au traitement

- Analyse post hoc du protocole I du DRCR.net

Factors Associated With Changes in Visual Acuity and Central Subfield Thickness at 1 Year After Treatment for Diabetic Macular Edema With Ranibizumab

Susan B. Bressler, MD; Haijing Qin, MS; Roy W. Beck, MD, PhD; Kakarla V. Chalam, MD; Judy E. Kim, MD; Michele Melia, ScM; John A. Wells III, MD; for the Diabetic Retinopathy Clinical Research Network

- 4 profils de réponse

La réponse initiale au traitement

Bon Répondeurs 50%	Tachyphylaxie 15%	Répondeurs Tardifs : 12%	Mauvais Répondeurs 23%

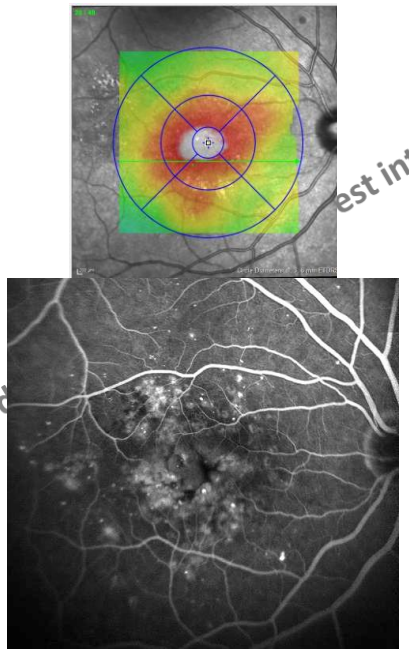
Change in Visual Acuity From Baseline to 1 Year*	Categorization of OCT CSF Thickness Improvement of at least 20% (1-step reduction of logOCT[I]) from Baseline			
	(A) Early and Consistent	(B) Early but Inconsistent	(C) Slow and Variable	(D) Non-responder
	N=143	N=43	N=36	N=66
Improved ≥15 Letters	60 (42%)	11 (26%)	5 (14%)	5 (8%)
Improved 14-10 Letters	32 (22%)	12 (28%)	7 (19%)	8 (12%)
Improved 9-5 Letters	33 (23%)	10 (23%)	10 (28%)	18 (27%)
Within ±4 Letters	14 (10%)	5 (12%)	12 (33%)	24 (36%)
Worsened 5-9 Letters	2 (1%)	4 (9%)	0	8 (12%)
Worsened 10-14 Letters	1 (1%)	1 (2%)	1 (3%)	2 (3%)
Worsened ≥15 Letters	1 (1%)	0	1 (3%)	1 (2%)
Median (25^{th}, 75^{th} Quartiles)	+12 (+7, +17)	+11 (+6, +15)	+8 (+3, +11)	+4 (-1, +8)
Mean ± SD	+13 ± 9	+9 ± 9	+7 ± 11	+4 ± 9

La sévérité de la rétinopathie

- Patients traités par PPR ont moins de chance d'obtenir une AV >20/40 (RISE & RIDE)
- RD proliférante associée à un moindre gain d'AV (DRCR.net protocole I)

La diffusion en angiographie à la fluorescéine

- The type of DME on FA (focal, diffuse or mixed) did not affect either VA gains or changes in CRT (DRCR.net protocole I)



Les exsudats rétiniens

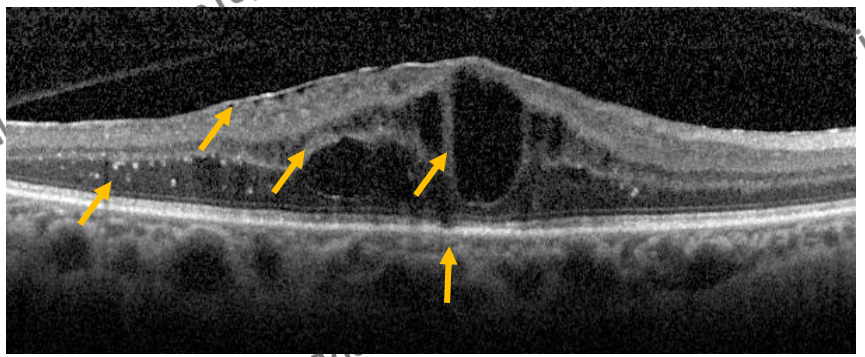
- Hard exudates in the macula did not seem to affect visual outcomes except in the laser group
(RISE / RIDE)

- Hard exsudates correlate strongly with reduction in central subfield thickness
(DRCR.net protocole I)

Critères prédictifs de l'OCT

Anomalies de l'interface

Taille et localisation des kystes



Points hyperréflectifs

Désorganisation de la rétine interne

Altérations de la rétine externe

Fluide intra et sous-rétinien

- Fluide intra-rétinien
  - Peu d'impact chez les patients traités par anti-VEGF
  - Réduction de l'AV ≥ 15 lettres chez les patients traités par laser ds RISE/RIDE

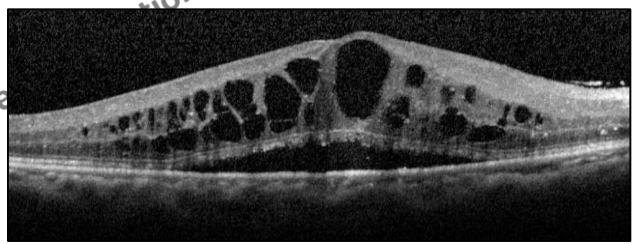
- Décollement séreux rétinien
  - SRF predicted:
    - a final BCVA >20/40
    - visual gains ≥ 15 letters
    - a final CRT ≤ 250 (RISE/RIDE)
  - It was also found that in the sham group sub-macular fluid correlated with a loss of 15 letters or more.

A Systematic Correlation between Morphology and Functional Alterations in Diabetic Macular Edema

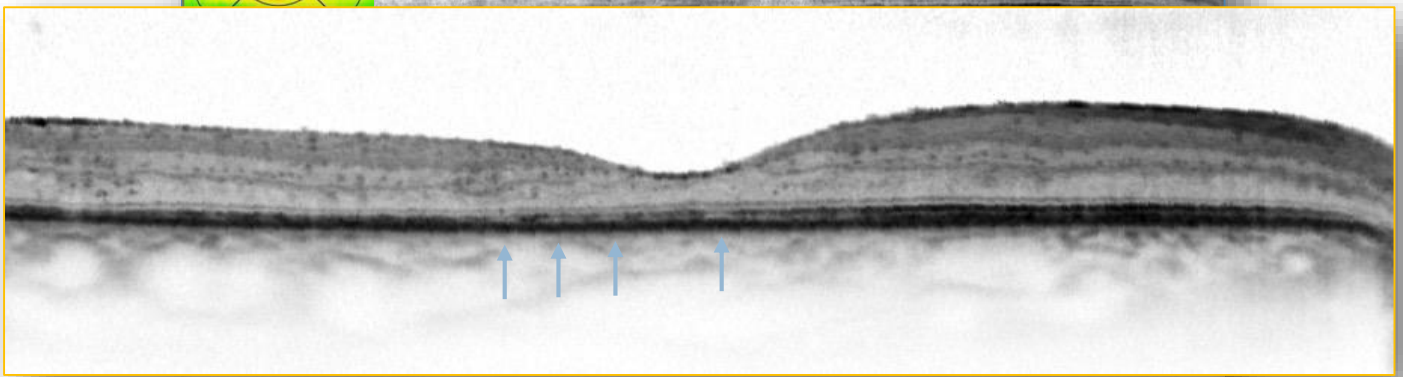
Gábor György Deák,[1,2] Matthias Bolz,[1] Markus Ritter,[1] Sonja Prager,[1] Thomas Benesch,[3] and Ursula Schmidt-Erfurth[1] for the Diabetic Retinopathy Research Group Vienna

IOVS 2011

SRF and large ONL cysts are the two morphologic changes with the greatest negative impact on VA

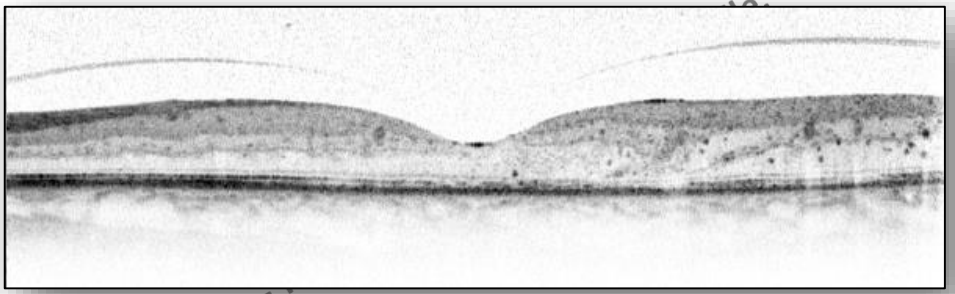


L'intégrité des couches externes



après 3 IVT . AV : 2/10 EMC : 225 µm

Atteinte des photorécepteurs



Relationship between Optical Coherence Tomography Retinal Parameters and Visual Acuity in Diabetic Macular Edema

Tarek Alasil, MD, Pearse A. Keane, MRCOphth, MSc, Jared F. Updike, MS, Laurie Dustin, MS, Yanling Ouyang, MD, Alexander C. Walsh, MD, Srinivas R. Sadda, MD

Ophthalmology 2010

PR outer segment thickness correlated with VA

RELATIONSHIP BETWEEN PHOTORECEPTOR OUTER SEGMENT LENGTH AND VISUAL ACUITY IN DIABETIC MACULAR EDEMA

FARZIN FOROOGHIAN, MD, MSc,* PAUL F. STETSON, PhD,†
SCOTT A. MEYER, PhD,† EMILY Y. CHEW, MD,*
WAI T. WONG, MD, PhD,‡ CATHERINE CUKRAS, MD, PhD,*
CATHERINE B. MEYERLE, MD,* FREDERICK L. FERRIS, III, MD*

Retina 2010

The Association Between Percent Disruption of the Photoreceptor Inner Segment–Outer Segment Junction and Visual Acuity in Diabetic Macular Edema

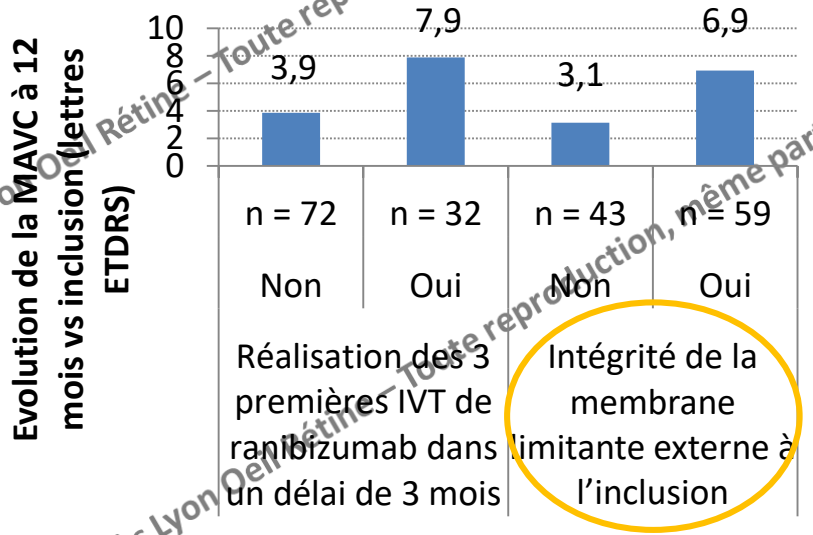
ANJALI S. MAHESHWARY, STEPHEN F. OSTER, RITCHIE M. S. YUSON, LINGYUN CHENG, FRANCESCA MOJANA, AND WILLIAM R. FREEMAN

Am J Ophthalmol 2011

Photoreceptor IS/OS integrity : correlated with VA

Etoile

Acuité visuelle moyenne au cours des 12 mois - analyses en sous-groupes



D'après L Kodjikian SFO 2017

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Réponse aux corticoïdes

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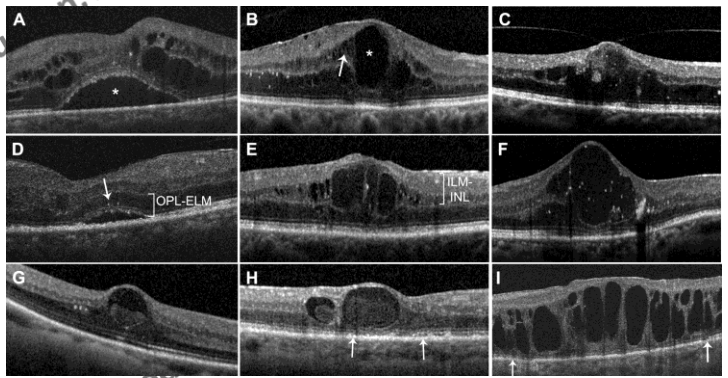
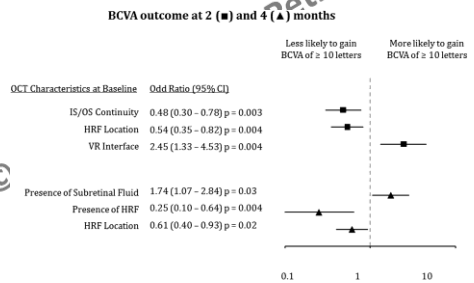
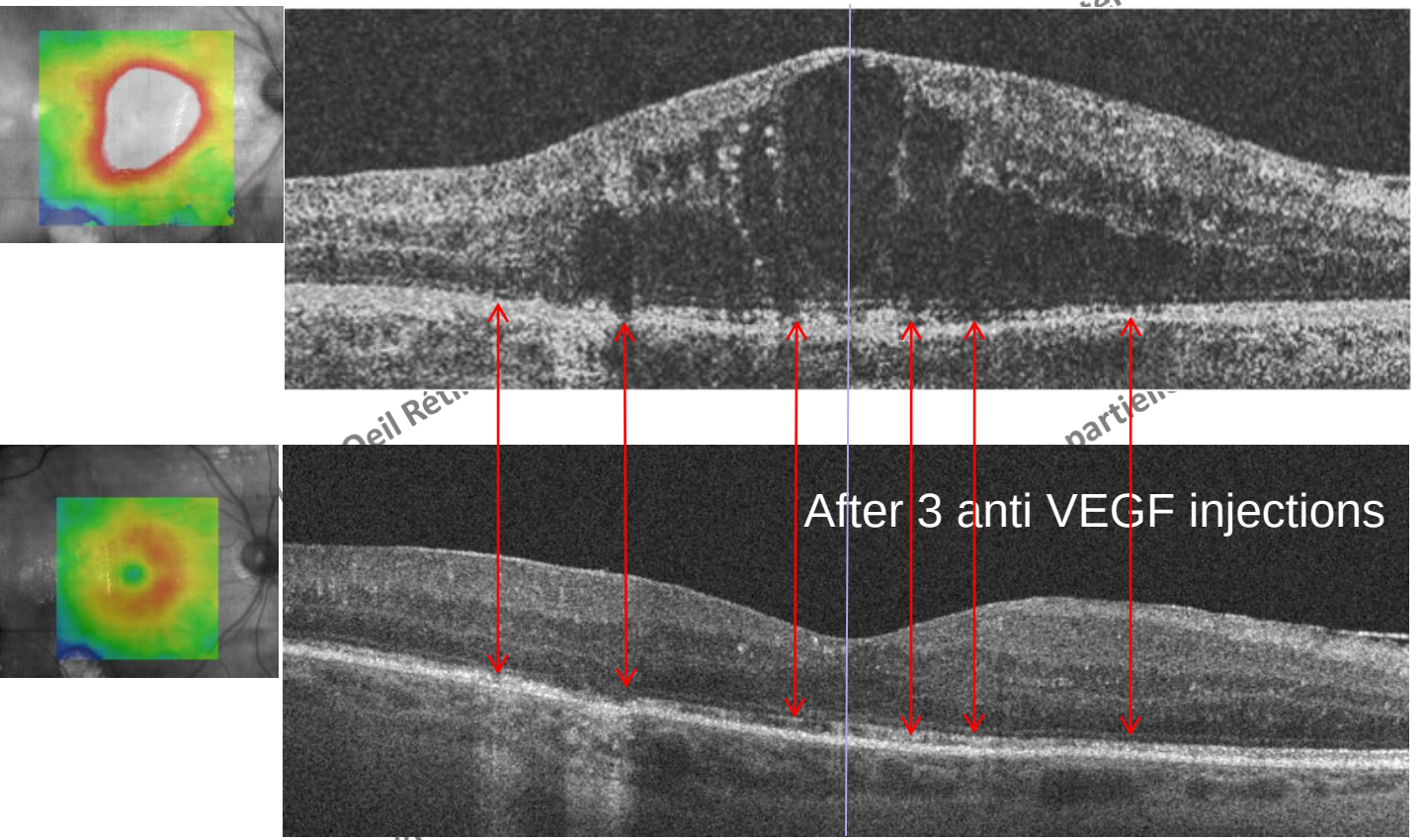
Optical Coherence Tomography Biomarkers as Functional Outcome Predictors in Diabetic Macular Edema Treated with Dexamethasone Implant

Dinah Zur, MD,[1,2] Matias Iglicki, MD,[2,3] Catharina Busch, MD,[3] Alessandro Invernizzi, MD,[4] Miriana Mariussi, MD,[5] Anat Loewenstein, MD,[1,6] for the International Retina Group





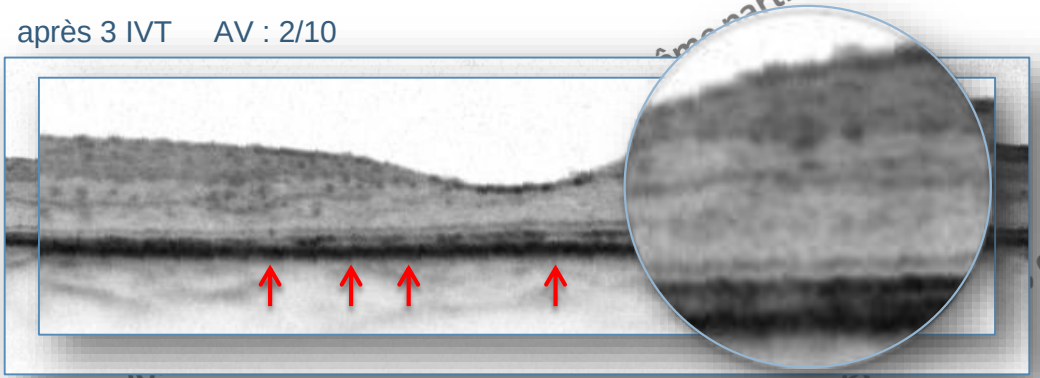
Conclusions: Spectral-domain OCT is useful in identifying various imaging findings in DME. Among eyes with DME, those with submacular fluid, no HRF, and a continuous IS-OS layer responded better to DEX implants than those without these features. These findings call for further study of combinations of OCT and metabolic biomarkers. *Ophthalmology 2017;■:1–9 © 2017 by the American Academy of Ophthalmology*

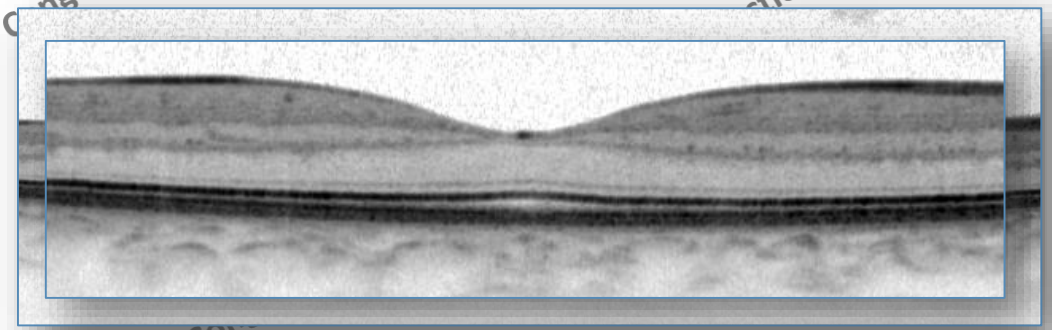


Limites : difficultés d'évaluer l'intégrité des structures rétiniennes dans l'OM

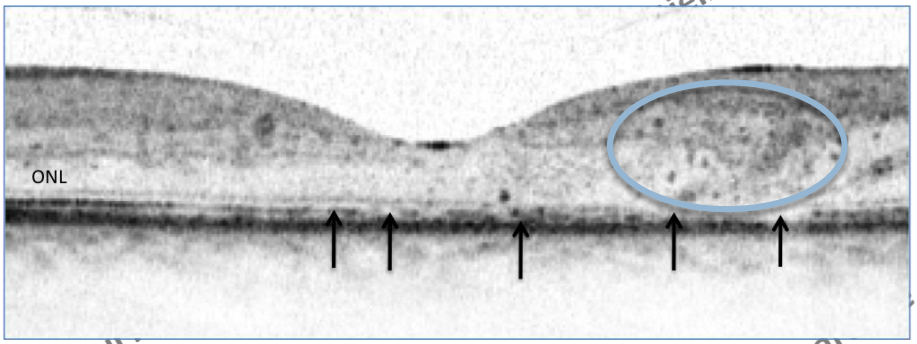
La désorganisation de la rétine interne

après 3 IVT AV : 2/10





La désorganisation de la rétine interne



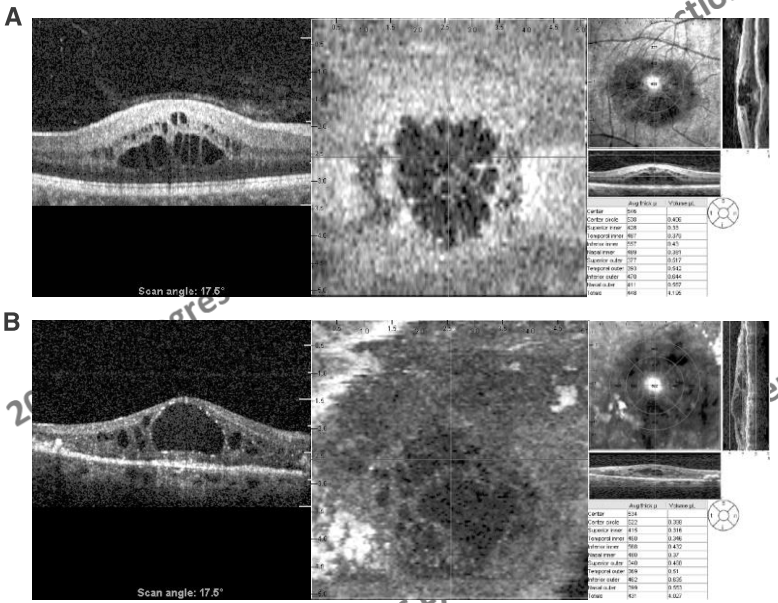
Après OM chronique

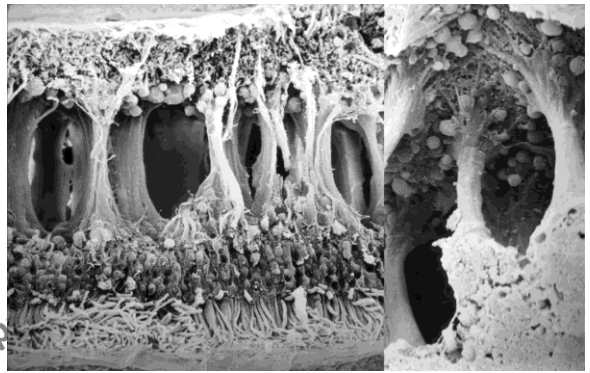
- Several retrospective studies found DRIL to correlate with BL VA.
- DRIL affecting ≥50% of the 1 mm central retinal zone was associated with worse VA in all eyes, eyes with current oedema, and eyes with resolved oedema
- In addition, it was found that an increase in DRIL was associated with worsening outcomes: early 4-month change in DRIL extent predicted VA change from baseline to 1 year

Optical Coherence Tomography May Be Used to Predict Visual Acuity in Patients with Macular Edema

Lucia Pelosini,[1] *Christopher C. Hull,*[2] *James F. Boyce,*[1] *Dominic McHugh,*[3] *Miles R. Stanford,*[1] *and John Marshall*[1]

IOVS 2011





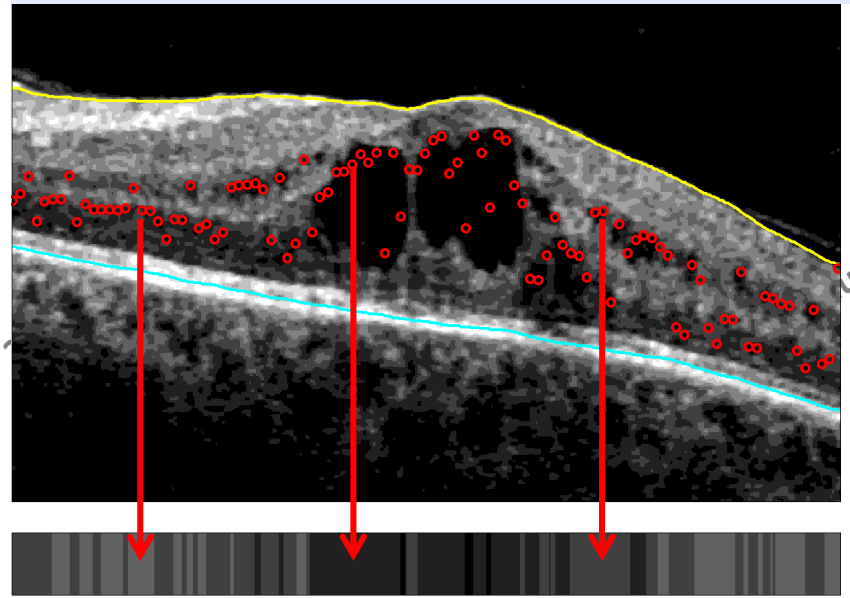
Quantification du tissu rétinien résiduel

Technique de la projection de l'intensité minimale

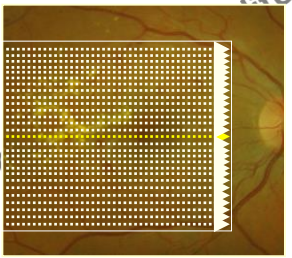
OCT en face: Pour chaque A-scan, intensité minimale (o) identifiée

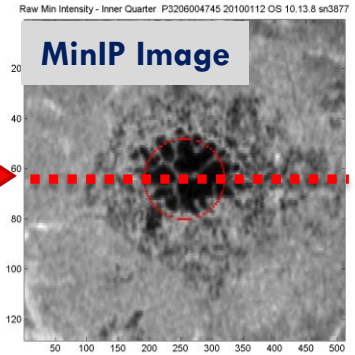
Résultats projetés sous forme d'un ruban de données pour chaque B-scan

Juxtapostion des rubans → MinIP



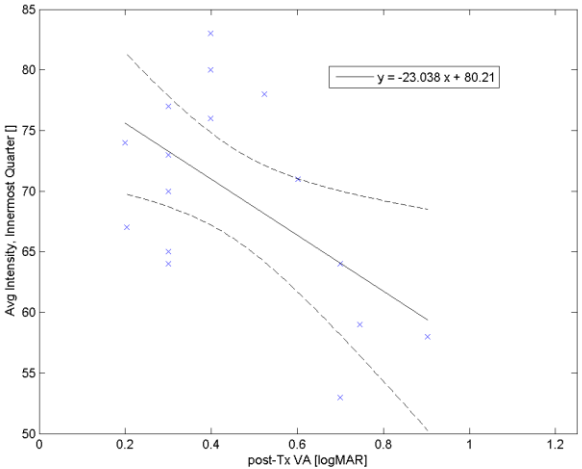
Cirrus™ S-CT

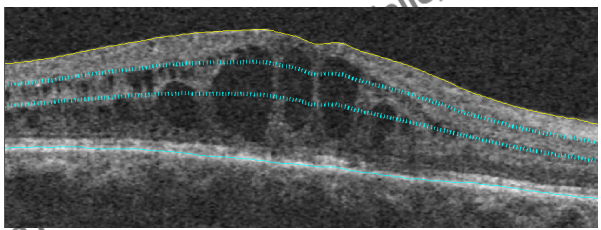




L'intensité moyenne dans la **rétine interne** avant IVT est corrélée à l'AV après IVT

(r = -0.57, P = 0.02)





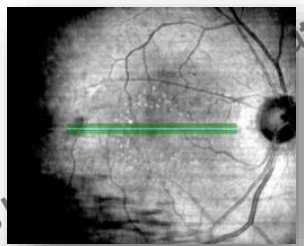
Retina

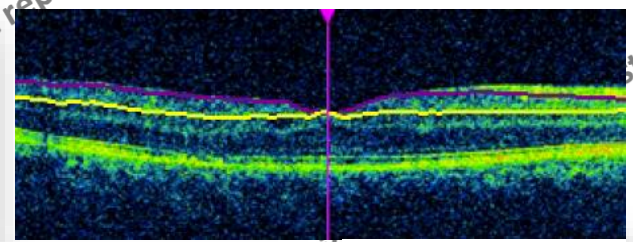
Correlation Between Ganglion Cell Layer Thinning and Poor Visual Function After Resolution of Diabetic Macular Edema

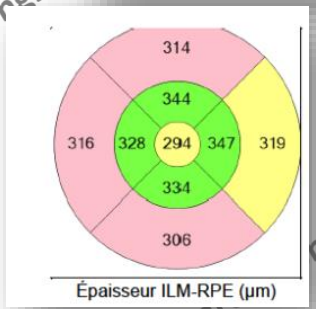
Sophie Bonnin, Ramin Tadayoni, Ali Erginay, Pascale Massin, and Bénédicte Dupas

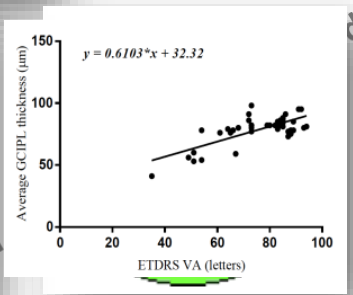
Service d'Ophtalmologie, Hôpital Lariboisière, AP-HP, Université Paris 7-Sorbonne Paris Cité, Paris, France

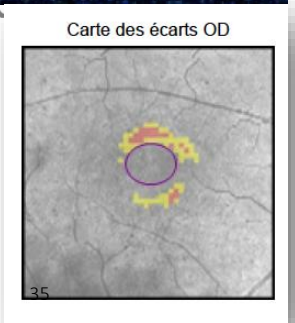
2015



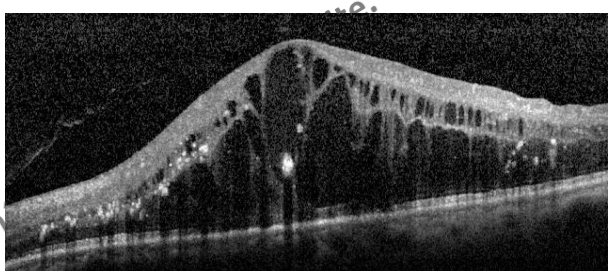








Points hyperréflectifs

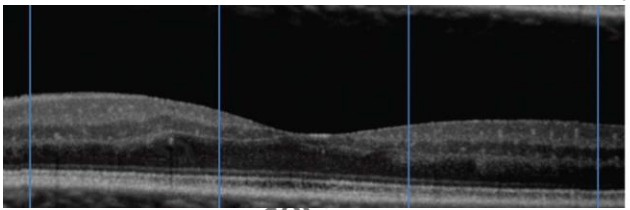


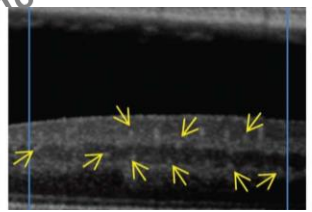
- Origine?
  - Lipoprotéines
  - Dégénerescence PR
  - Cellules microgliales activées
- Diminution après anti-VEGF
- Corrélation au résultat fonctionnel

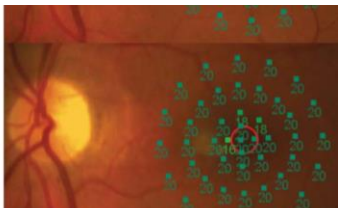
HYPERREFLECTIVE RETINAL SPOTS AND VISUAL FUNCTION AFTER ANTI-VASCULAR ENDOTHELIAL GROWTH FACTOR TREATMENT IN CENTER-INVOLVING DIABETIC MACULAR EDEMA

STELA VUJOSEVIC, MD, PHD,* MARIANNA BERTON, MD,* SILVIA BINI, MD,* MARGHERITA CASCIANO, MD,* FABIANO CAVARZERAN, SCD,* EDOARDO MIDENA, MD, PHD*†

RETINA 0:1–11, 2015

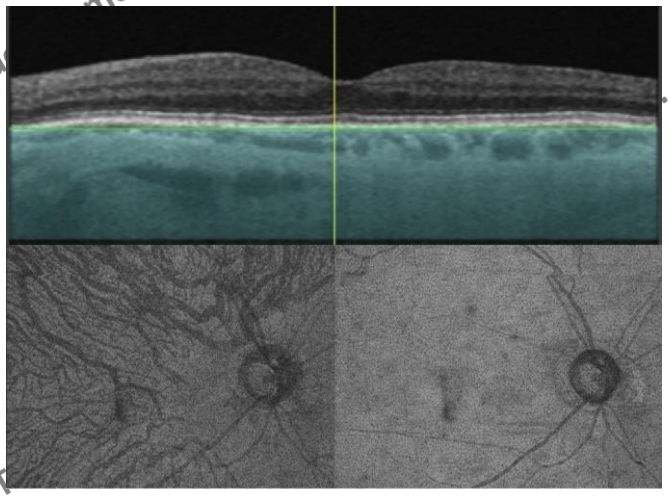






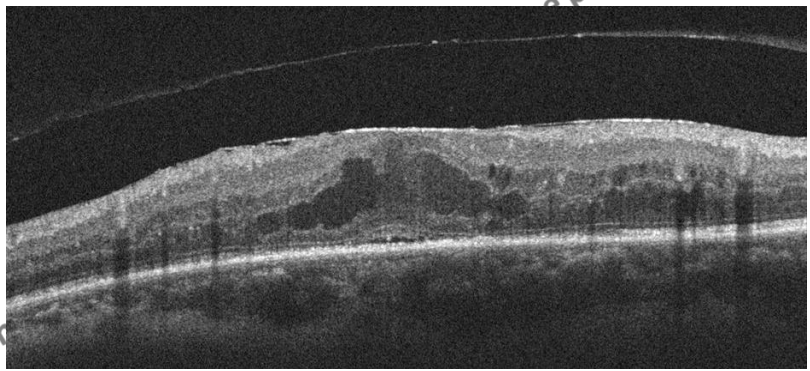
Épaisseur choroidienne

- Choroïde plus épaisse associée à un meilleur résultat anatomique et fonctionnel (Rayess et al)
- Diminution de l'épaisseur choroïdienne sous anti-VEGF (Yiu et al)



Membrane épirétinienne

- Absence de MER: facteur de meilleure réponse
  - DRCR.net protocol I: Patients having no evidence of ERM achieving an additional 4 letter improvement



Critères prédictifs de l'OCT

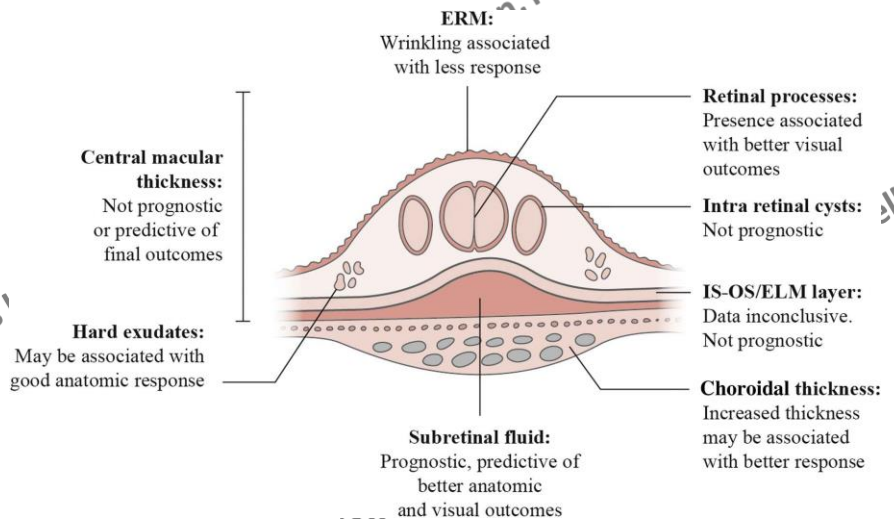
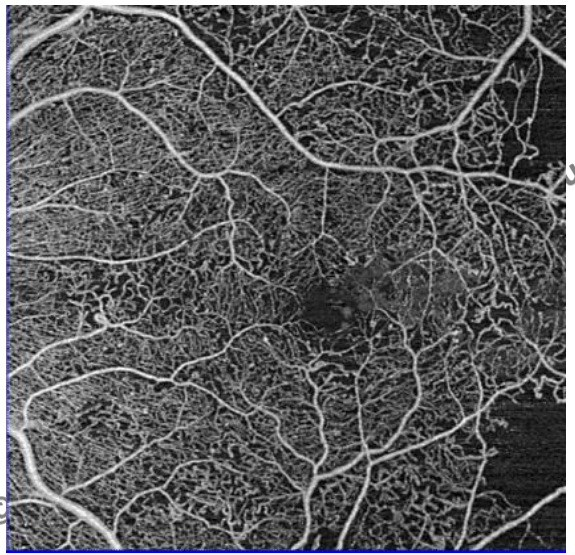
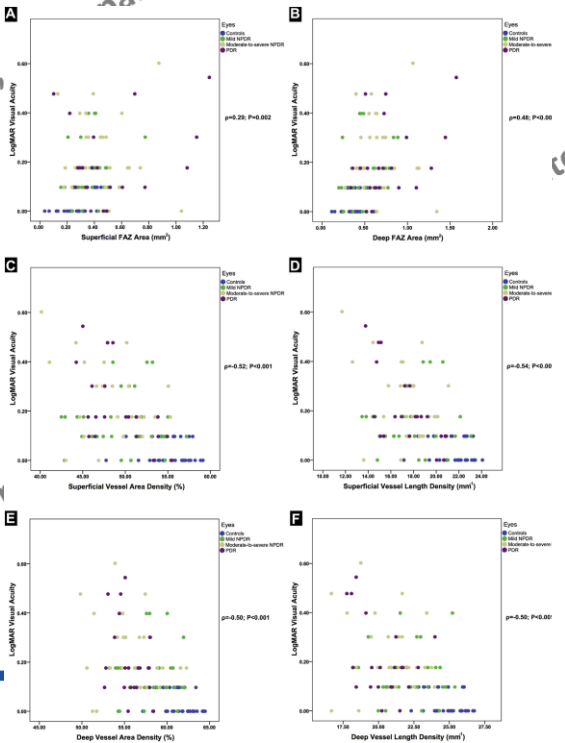


Figure 1 Illustration showing the various anatomic and optical coherence tomography findings that predict response to anti-vascular endothelial growth factor (VEGF) therapy. ELM, external limiting membrane; ERM, epiretinal membrane; IS-OS, inner segment-outer segment.

Vers de nouveaux critères morphologiques?

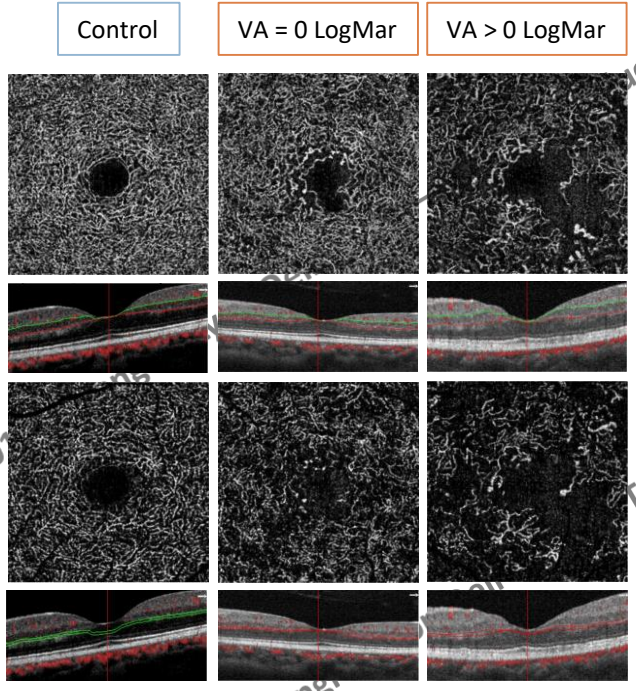


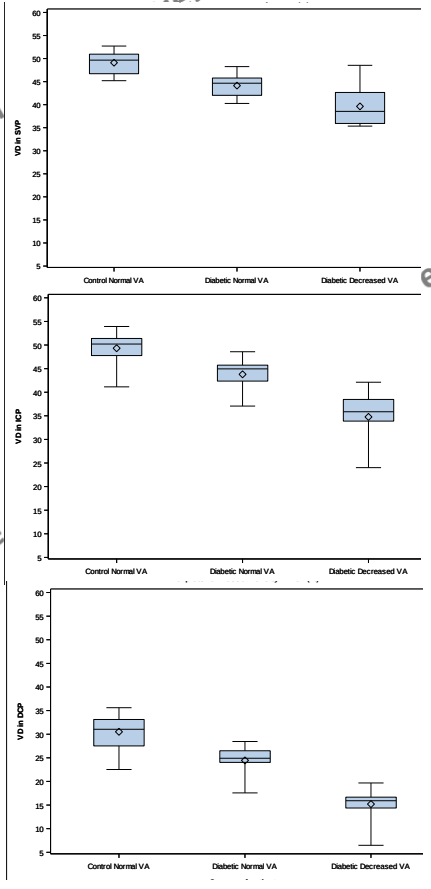


Quantification of Diabetic Macular Ischemia Using Optical Coherence Tomography Angiography and Its Relationship with Visual Acuity

Wasim A. Samara, MD, Abtin Shahlaee, MD, Murtaza K. Adam, MD, M. Ali Khan, MD, Allen Chiang, MD, Joseph I. Maguire, MD, Jason Hsu, MD, Allen C. Ho, MD

Vers de nouveaux critères morphologiques?





Minvielle W, Dupas B. Submitted to JAMA

Vers de nouveaux critères morphologiques?

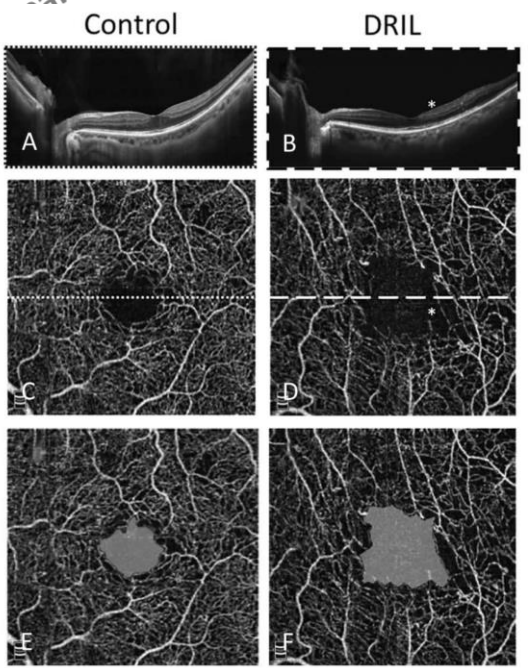
OPTICAL COHERENCE TOMOGRAPHY ANGIOGRAPHY TO DETECT MACULAR CAPILLARY ISCHEMIA IN PATIENTS WITH INNER RETINAL CHANGES AFTER RESOLVED DIABETIC MACULAR EDEMA

HAMID-REZA MOEIN, MD,* EDUARDO A. NOVAIS, MD,*† CARL B. REBHUN, BA,*
EMILY D. COLE, BSc,* RICARDO N. LOUZADA, MD,*‡ ANDRÉ J. WITKIN, MD,*
CAROLINE R. BAUMAL, MD,* JAY S. DUKER, MD,* NADIA K. WAHEED, MD, MPH*

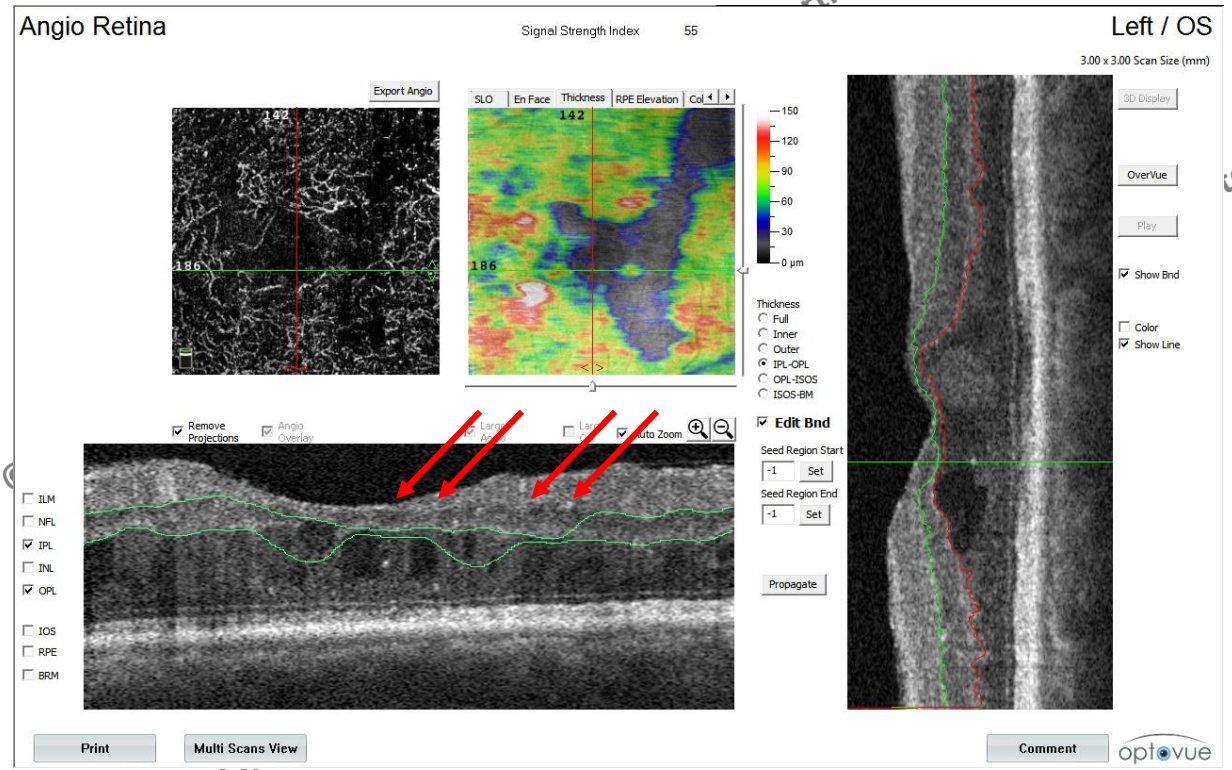
Results: Nine eyes with DRIL and resolved diabetic macular edema were compared with 15 control eyes without DRIL and resolved diabetic macular edema. Area of ischemia on OCTA scans corresponded to the area of DRIL as determined on OCT B scans. The foveal avascular zone area in full retina as well as superficial and deep retinal plexuses OCTA slabs were significantly larger in patients with DRIL as compared to those without DRIL ($P = 0.005$, $P < 0.001$, and $P = 0.004$, respectively). The larger foveal avascular zone in full retinal segmentation ($r = 0.72$, $P = 0.03$) and superficial plexus ($r = 0.74$, $P = 0.02$) were positively correlated with lower visual acuity.

Conclusion: Optical coherence tomography angiography can visualize retinal ischemia in patients with and without DRIL. Correspondence of impaired blood flow with DRIL suggests that retinal ischemia and loss of normal vasculature contributes to DRIL.

RETINA 0:1–8, 2017



Vers de nouveaux critères morphologiques?

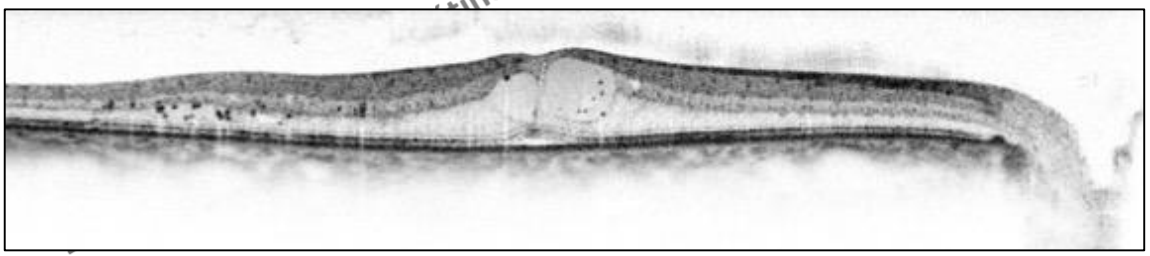


Critères prédictifs du traitement de l'OMD: *à retenir*

- L'AV initiale est le principal déterminant
- Facteurs généraux: âge jeune, sexe masculin, durée du diabète

- Biomarqueurs OCT:
  - Absence de MER, TVM
  - Intégrité de la zone ellipsoïde et MLE
  - Absence de désorganisation de la rétine interne (DRIL)
  - Absence de points hyperréflectifs intrarétiniens
  - Présence d'un DSR

- Intérêt du traitement précoce!



MERCI POUR VOTRE ATTENTION

aude.couturier@aphp.fr

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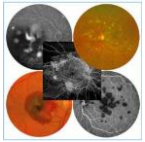
Hôpital Lariboisière (AP-HP)
Université Paris 7 (Sorbonne Paris Cité)

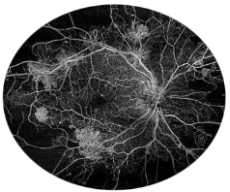


RÉTINE EN PRATIQUE

13ème Edition

Les nouveaux

DILEMMES THÉRAPEUTIQUES



Vendredi 30 mars 2018

Maison de la Chimie - Paris

NOUVEAU

Sessions DPC validantes et rémunérées

Info et inscription : retine-en-pratique18.com