



Correlation of Response to Bevacizumab Treatment Between the First and Second Treated Eyes in Diabetic Macular Edema

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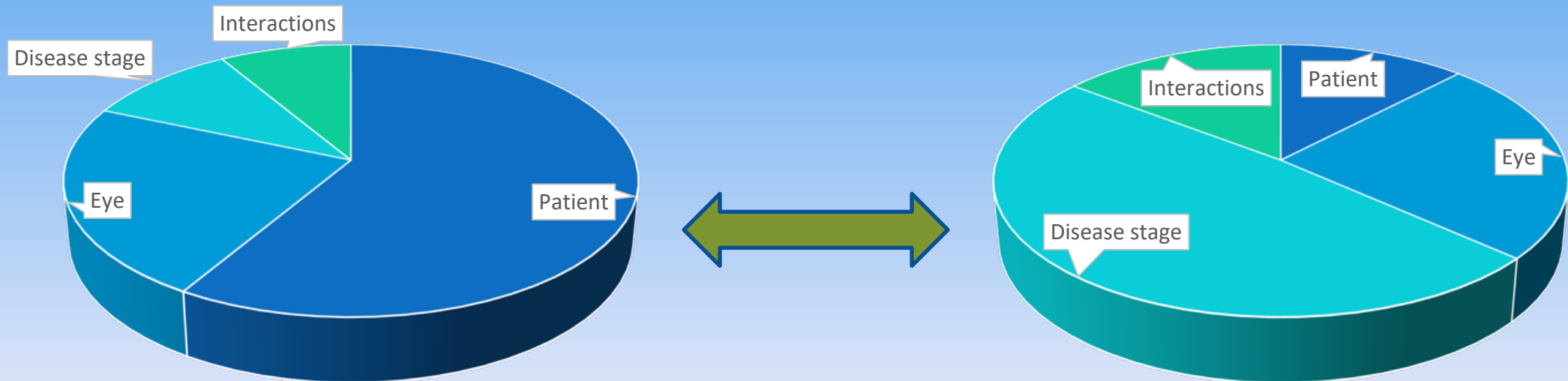
Summary

- Retrospective analysis of 66 eye (33 pts.) under bilateral bevacizumab tx. for DME
- 1st eye outcome correlates with/predict 2nd eye outcome?
 - Overall correlation exist among eyes under anti-VEGF therapy
 - Diagnostic accuracy
 - Poor for 1st line bevacizumab
- 1st eye outcome cannot exclusively guide selection of compound for 2nd eye tx. in DME
- Studying bilateral anti-VEGF therapy is important to identify and quantify factors modulating tx. outcome

Aim

- Evaluate correlation of anti-VEGF tx. outcome in DME between fellow eyes
 - Assess patient-level effect on anti-VEGF tx. outcome
 - Select compound for 2nd eye tx.

Anti-VEGF Treatment Outcome



Methods

- Retrospective, consecutive
- Inclusion
 - Bilateral DME
 - Bilateral anti-VEGF therapy with bevacizumab
 - Data collected: demographics, exams (EMR), tx., SD-OCT
- Statistical analysis via SPSS

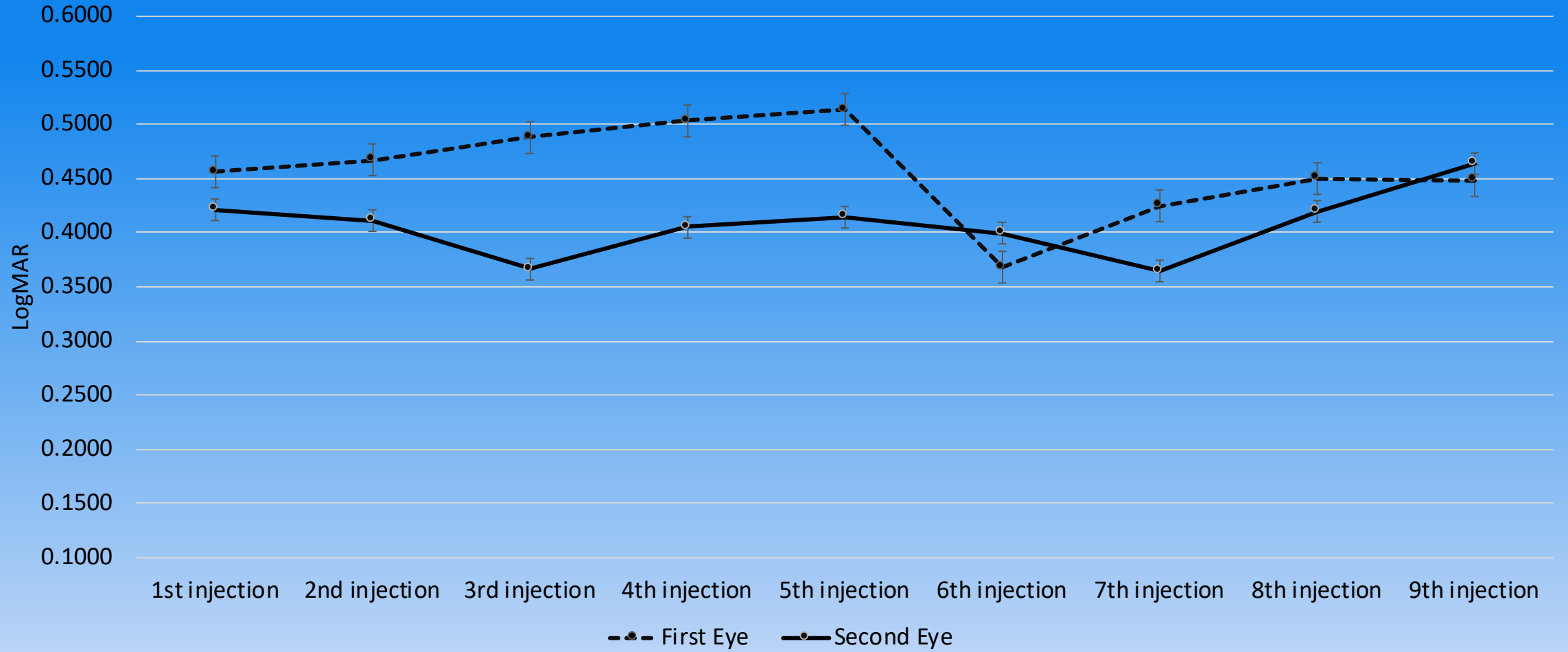
Results: Demographics

- Both eyes of 33 patients
- Gender: (Female/male) 17/16
- Age: 61.15 ± 9.93
- HbA1C%- 8.4 ± 2.09
- Follow-up: 13 ± 4.99 months
- Time differences of initial treatment between the eyes, months \pm SD: 1.53 ± 3.2

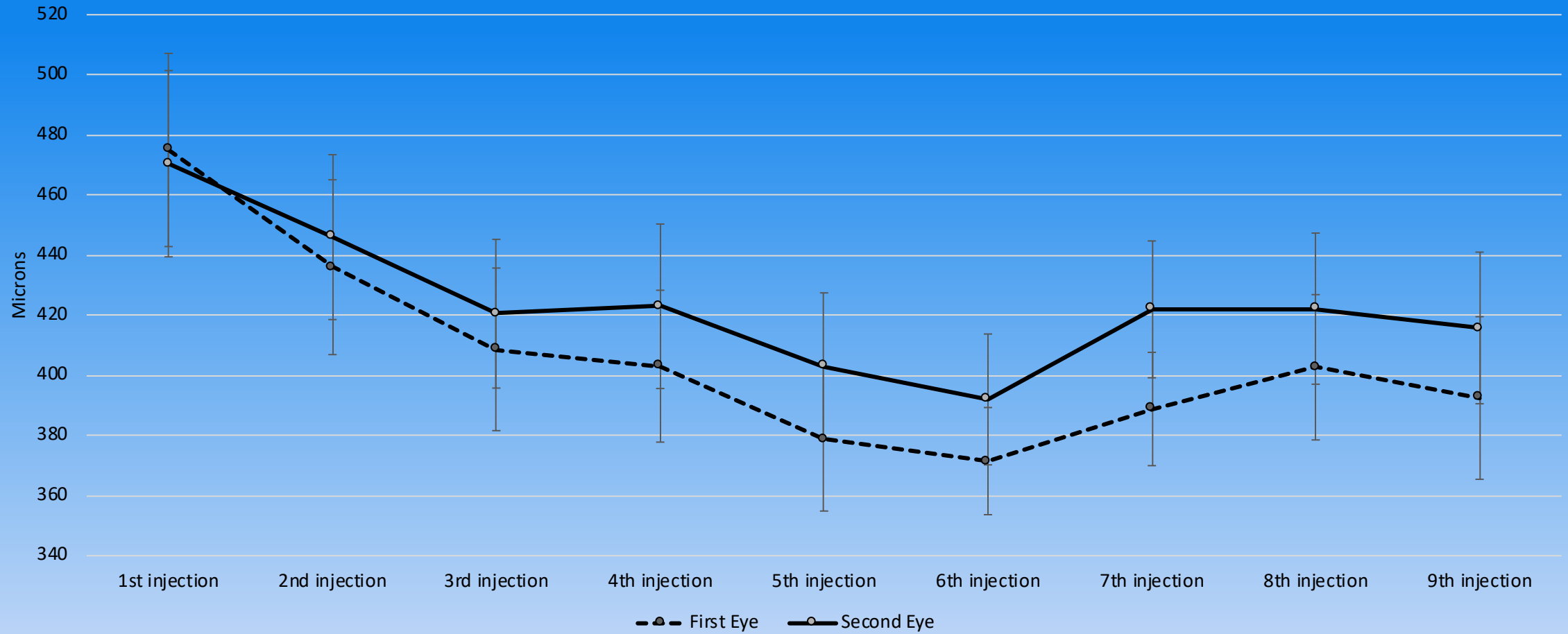
Baseline characterization (n=33)

	First eye	Second eye	P value
Vitreous interface			
Attached	15 (45.5)	14 (42.4%)	0.921
ERM	6 (18.2%)	6 (18.2%)	1
Macular edema			
Diffuse	8 (24.2%)	9 (27.3%)	0.705
Cystoid	21(63.6%)	18 (54.5%)	0.618
NSD + Diffuse	4 (12.1%)	6 (18.2%)	0.859
DRIL	10 (30.3%)	8 (24.2%)	0.887
ELM abnormality	9 (27.3%)	6 (18.2%)	0.713
Hyper-reflective foci	25 (75.8%)	27 (81.8%)	0.341
Ellipsoid zone disruption	9 (27.3)	7 (21.2%)	0.387
Intra-retinal cysts	33 (100%)	33 (100%)	1
Sub-retinal fluid	6 (18.2%)	4 (12.1%)	0.859

Visual Acuity (n=33)



Central Subfield Thickness (n=33)



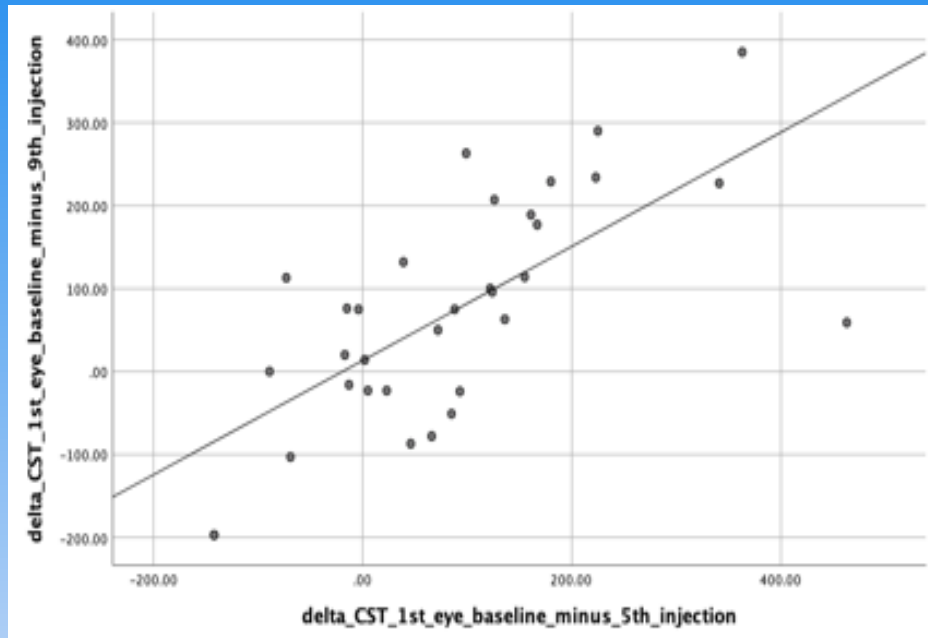
Regression Analysis (prediction models)

- First step: IN EACH EYE, linear regression to predict the final reduction of CST by the outcome of delta CST after 3 or 5 injections comparing baseline (of the same eye); in the first eye the outcome of CST at the end of the follow up can be predicted after 5 injections. The 2nd eye didn't show correlation.
- Second analysis: BETWEEN the eyes: multivariate analysis and logistic regression, the model couldn't predict the treatment outcome of the second eye based on the outcome of the first treated eye.

Linear Regression Model {specifically per eye}

First eye

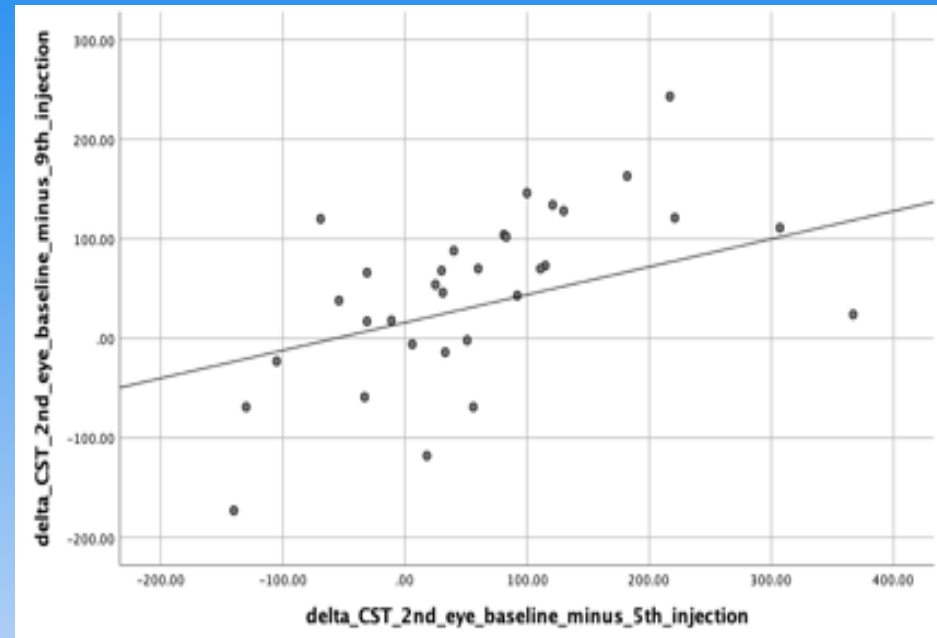
- Final CST reduction predicted after 5 injections



- Regression equation= $13.2 + 0.688X$
- $R^2=0.4781$, $p=0.001$

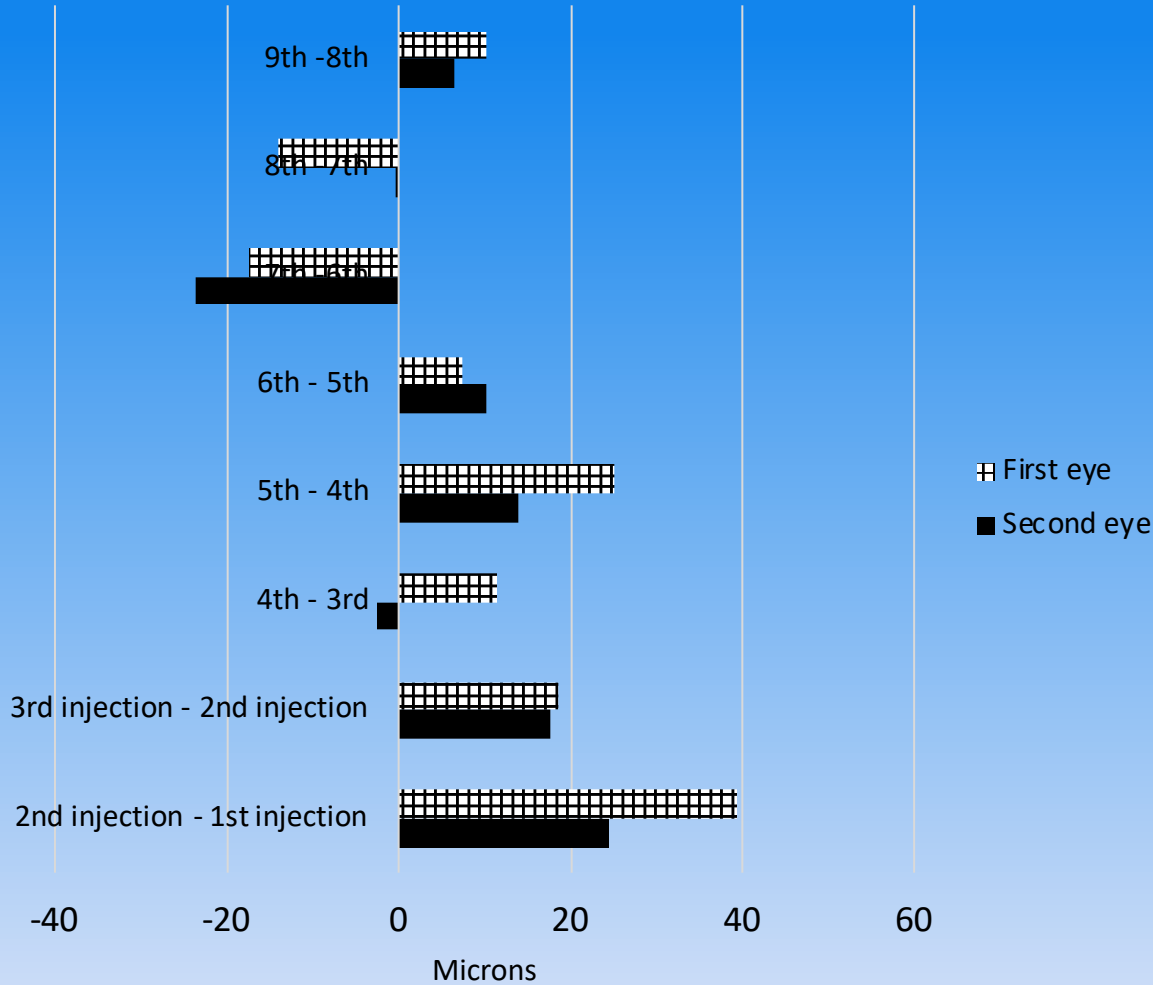
Second eye

- Final 2nd eye CST reduction can't predict following 3 or 5 injections



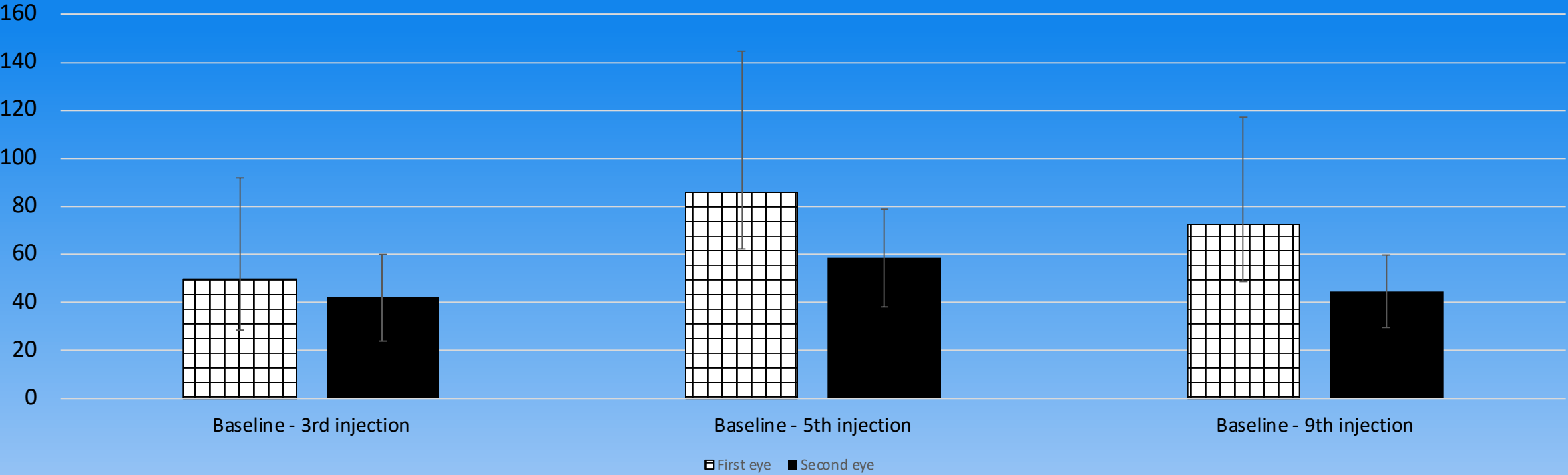
- Regression equation= $15.87 + 0.28X$
- $R^2=0.375$, $p=0.12$

Delta CST n=33



	Correlation coefficient	P value
Baseline – 2 nd injection	0.437	0.018
2 nd injection – 3 rd injection	0.087	0.665
3 rd injection – 4 th injection	0.121	0.533
4 th injection – 5 th injection	0.195	0.293
5 th injection – 6 th injection	0.101	0.581
6 th injection – 7 th injection	0.132	0.465
7 th injection – 8 th injection	0.016	0.930
8 th injection – 9 th injection	0.109	0.546

Delta CST comparing to baseline n=33

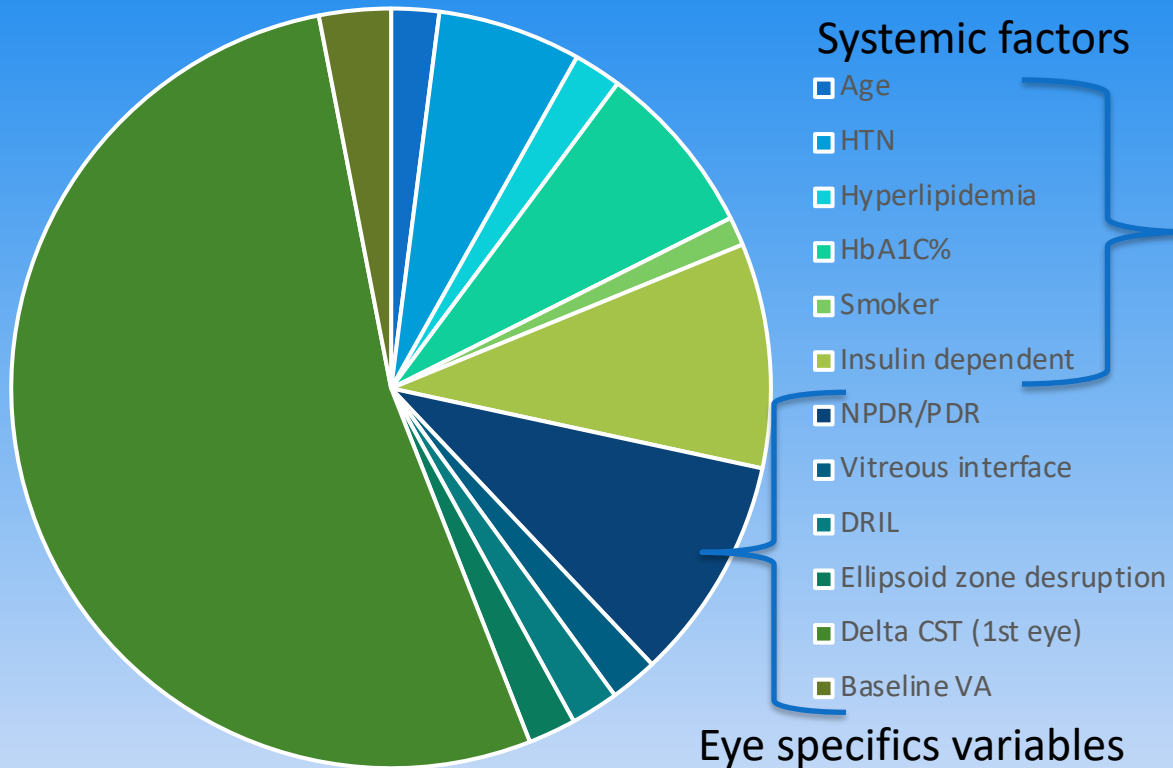


	Correlation coefficient	P value
Baseline – 3 rd injection	0.249	0.185
Baseline – 5 th injection	0.130	0.479
Baseline – last injection	0.163	0.365

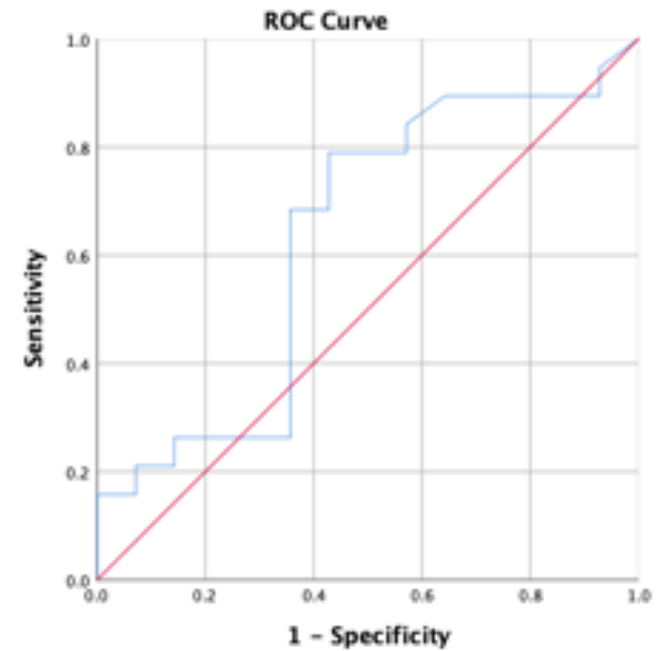
Diagnostic Accuracy of 1st Eye Outcome for Prediction of 2nd Eye Response

Predictive Factor	Prediction	Positive Predictive Value	Negative Predictive Value	Sensitivity	Specificity
Reduction of CST at month 3 in the 1st eye as a predictor for reduction of CST in the second eye at month 3					
>5% CST reduction in 1 st eye at month 3	>10% CST reduction in 2 nd eye at month 3	57.9%	81.8%	84.6%	52.9%
>10% CST reduction in 1 st eye at month 3	>10% CST reduction in 2 nd eye at month 3	46.7%	60.0%	53.8%	52.9%
Reduction of CST at month 9 in the 1st eye as a predictor for reduction of CST in the second eye at month 9					
>5% CST reduction in 1 st eye at month 9	>10% CST reduction in 2 nd eye at month 9	71.428%	66.666%	78.947%	57.142%
>10% CST reduction in 1 st eye at month 9	>10% CST reduction in 2 nd eye at month 9	73.684%	64.285%	73.684%	64.285%

Relative Contribution of the Predictors to the Multiple Regression Model (Systemic vs. Eye variables)



ROC and AUC 2nd eye results at the end of the follow up predicted by the results of 1st eye

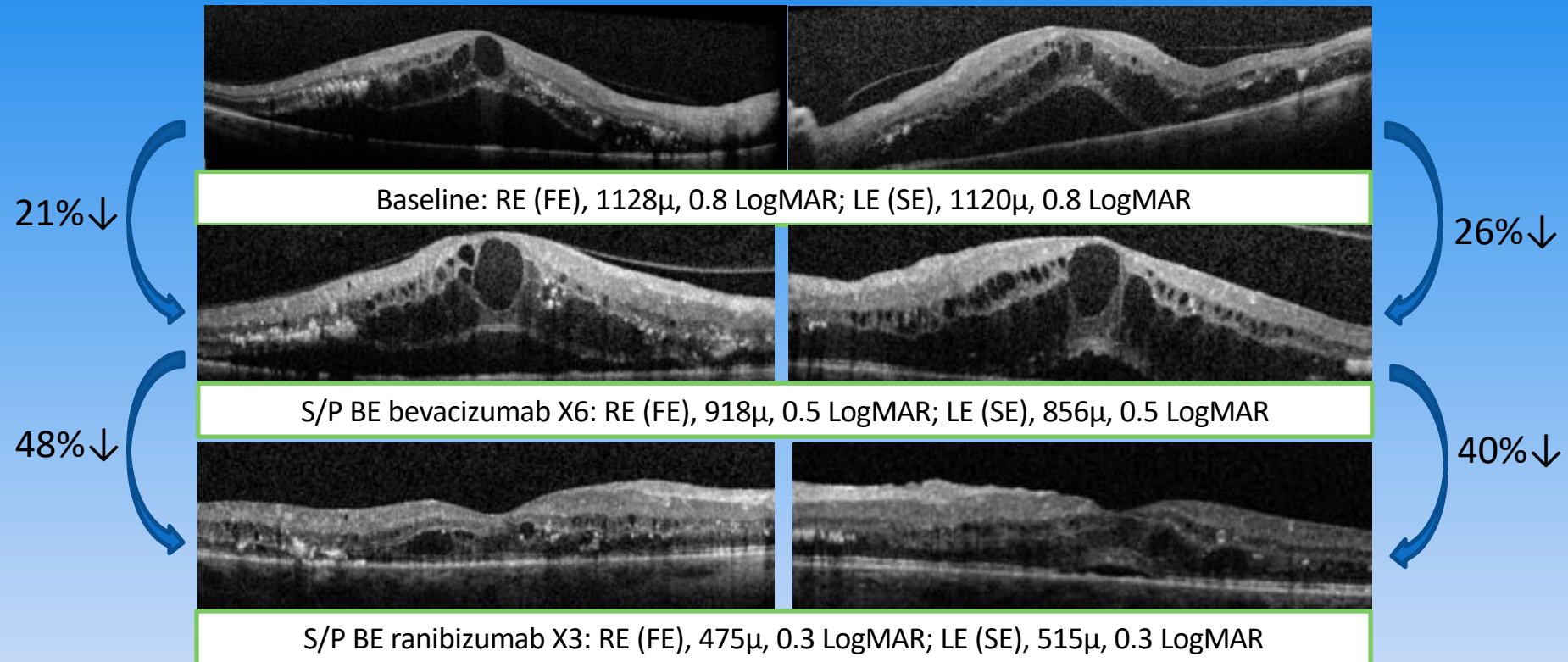


Diagonal segments are produced by ties.

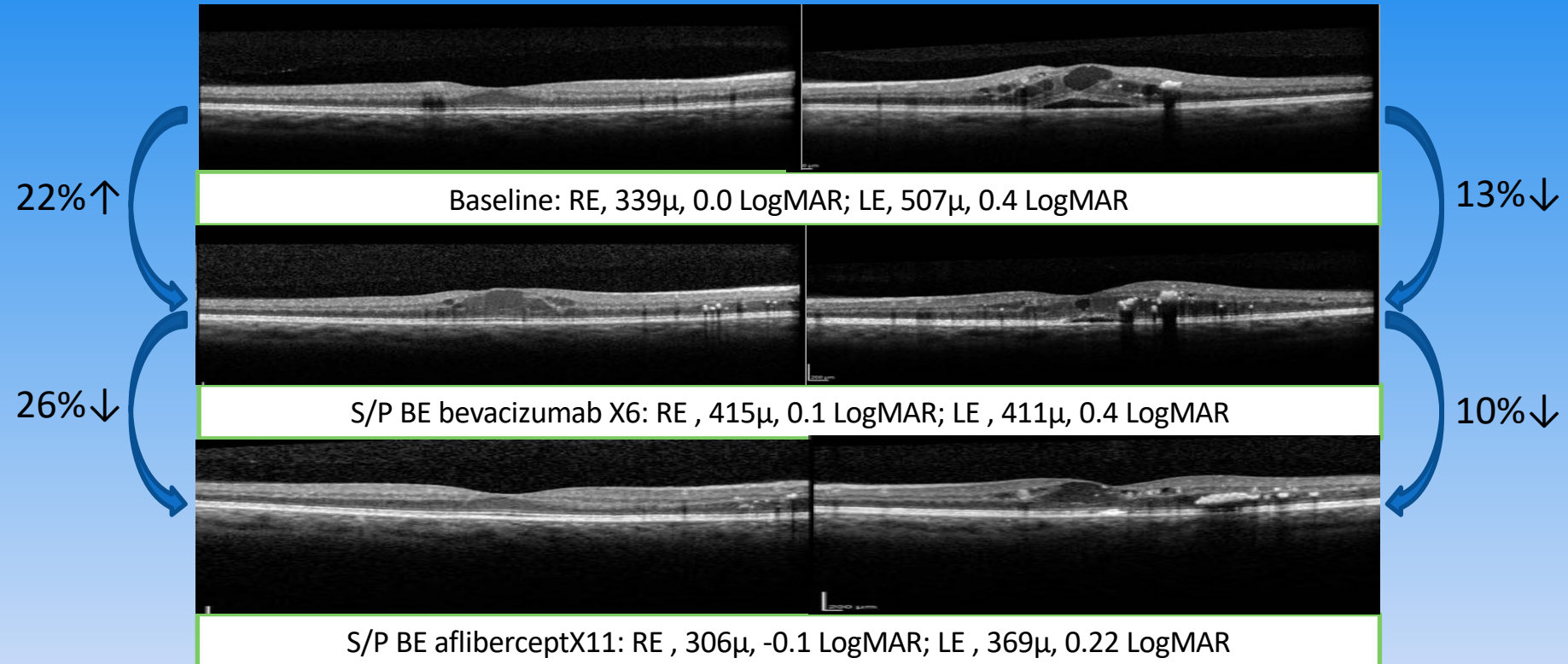
Area Under the Curve

Area	Std. Error ^a	Asymptotic Sig. ^b	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
0.632	0.103	0.202	0.430	0.834

DME Under Bilateral Anti-VEGF Therapy - case #1



DME Under Bilateral Anti-VEGF Therapy - case #2



Caveats of Study

- Retrospective
- Clinic setting
- Limited n
- Choice of threshold affects results
- Missing long-term data

Summary of Study

- Retrospective analysis of 66 eye (33 pts.) under bilateral anti-VEGF tx. for DME
- 1st eye outcome correlates with/predict 2nd eye outcome?
 - Overall correlation exist among eyes under anti-VEGF therapy
 - Poor diagnostic accuracy

Previous Works - Symmetry of Fellow Eye Response

- Retrospective data on 36 eyes (18 pts)- bilateral x3 IVR for DME (Guillard et al. Acta Ophthalmol 2016)
 - Favorable response >10% reduction in CST
 - Positive correlation between fellow eyes for
 - VA response ($R(2) = 0.26, p = 0.03$)
 - CST response ($R(2) = 0.37, p = 0.01$)
 - Symmetric favorable CST&VA responses in 13 pts. (72%)
- Retrospective data on 56 eyes (28 pts.)- bilateral IVB for DME (Karth et al. Graefe Arch Clin Exp Ophthalmol 2014)
 - 21 % of CST reduction after IVB in 2nd eye explained by % CST change in 1st eye

Conclusions – Bilateral Treatment in DME

- 1st eye outcome cannot exclusively guide selection of compound for 2nd eye tx. in DME
- Studying bilateral anti-VEGF therapy is important to identify and quantify factors modulating tx. outcome



Thank You

