Table A2. Summary of studies assessing retinally induced aniseikonia for patients with various retinal disorders, showing patient demographics, magnitude of aniseikonia (positive aniseikonia values indicate macropsia and negative values indicate micropsia) and method of measurement, other visual symptoms, retinal imaging, intervention and outcomes.

Author, Publication Year, Study Type and Purpose	Retinal disorder	Demographics	Aniseikonia method and findings #	Other visual findings and/or symptoms reported	Retinal Imaging Findings (OCT)	Intervention	Outcome	Key points and conclusions
Benegas et al 1999[13] Retrospective case series To provide an explanation for binocular diplopia and the inability to fuse in patients with macular disease.	ERM (n=6) Vitreo macular traction (n=1)	n = 7 mean age 69.8 yrs FU variable	NAT All had ANK: Micropsia 2 (29%) Macropsia: 5 (71%) ANK mag: 9.6% (range 5% to 18%)	BCVA: logMAR 0.06 (20/23) Diplopia: 100% Strabismus: 100% Metamorphopsia: 100% Cyclotorsion: 43% Impaired stereopsis: 100%	NR	Optical and/or surgical	Response to both types of treatment was variable	Retinally induced aniseikonia can be a contributing factor for binocular diplopia and the inability to fuse with prisms in patients having macular disease. Surgical and/or optical treatment did not improve aniseikonia symptoms.
Ugarte et al 2005[14] Prospective case series To determine whether a computerized version of the NAT is a valid and reliable method to measure ANK and establish whether ANK occurs in patients with unilateral ERM with good BCVA.	ERM	n = 14 mean age 67.7 ± 14.4 yrs 9M, 5F FU NR	Computerized NAT All had ANK: Macropsia: 11 (79%) Micropsia: 3 (21%) ANK mag: V 6.4% (range 3% to 11%) H 7.1% (range 2% to 13%) ≥ 2% difference between H and V ANK (n = 8)	BCVA: logMAR 0.18 (20/30) Blurred vision: 36% Rivalry: 21% Diplopia: 14% Reading difficulty: 29% Impaired stereopsis: 14%	NR	NR	NR	ANK occurred in symptomatic patients with unilateral ERM. Most had macropsia in the affected eye. The amount of ANK was heterogeneous across the retinal area affected. Studies are needed to determine effect of surgical and other types of intervention on ANK and patients' symptoms.
Ugarte et al 2006[23] Prospective case series To describe horizontal and vertical ANK occurring in patients 6 - 7 months following surgical re-attachment for macula-off rhegmatogenous RD.	Re-attached RD	n = 4 mean age 59 ± 8 yrs 1M, 3F FU NR	Computerized NAT All had ANK 6-7 months following surgery All had micropsia ANK mag: H and V ANK 4.5% (range 1.5% to 9%) ≥ 3% difference b/w H and V ANK: n =3	BCVA: logMAR 0.52 ± 0.19 (20/66) Difficulty judging distances Reading difficulty Rivalry Asthenopia	Thickness of maculae including the fovea in each case was within normal limits 6-7 months following surgery	NR	NR	ANK with micropsia occurred in symptomatic patients 6-7 months following successful macula-off RD surgery. The amount of ANK was heterogeneous across the retinal area affected.
Rutstein 2012[15] Retrospective case series To report clinical findings for patients who developed binocular vision difficulties possibly attributed to retinally induced ANK.	Reattached RD (7) ERM (4) ARMD (1)	n = 12 mean age 69.6 yrs 11M, 1F FU variable	NAT or AI All had ANK: Micropsia: 7 (58%) Macropsia: 5 (42%) V ANK_0: 6.9% (range 1.7%-11.3%) H ANK_0:7.1% (range 1.5%-13.3%)	BCVA: logMAR range 0.00-0.40 (20/20 to 20/50) Metamorphopsia: 83% Diplopia: 83% Strabismus: 8% Cyclotorsion: 42% Impaired stereopsis: 100%	NR	Optical Bangerter filters	ANK symptoms persisted in most cases	Retinally induced ANK is an increasingly important contributing cause of binocular vision symptoms in the ageing population. Long-term studies on its incidence, clinical course, and most effective treatments are needed.
Okamoto et al 2014[16] Prospective interventional case series To quantify ANK before and after ERM surgery and to investigate the relationship between ANK and foveal microstructure.	ERM	n = 44 mean age 65.3 ± 9.8 yrs 20M, 24F FU 3 & 6 mos	NAT 40 (91%) had ANK: Micropsia: 1 (2%) Macropsia: 39 (89%) ANK mag: 6.2% ±4.5% (range -1% to 19.5%)	$BCVA_0$ logMAR 0.33 ± 0.20 (20/43)	Preoperative ANK was significantly correlated with pre-operative INL and GCL thickness and post-operative ANK was significantly correlated with post-operative INL thickness	Surgical	$BCVA_{3\,m}$: log MAR 0.17 ± 0.20 (20/30) $BCVA_{6\,m}$: log MAR 0.13 ± 0.19 (20/27) ANK_{3m}: 6.2% ± 4.5% (range-2.5% to 19%) ANK_{6m}: 6.5% ± 4.3% (range -1.5% to 17%)	Most patients with ERM had ANK with macropsia. ANK was not reduced 6 months following surgery despite thinning of all retinal layers. Preoperative INL thickness is a good indicator of the severity of ANK and can be used to predict its magnitude in patients that have undergone ERM surgery.
Okamoto et al 2014[24] Prospective case series To quantify ANK 6 months after surgery for RD (scleral buckling or vitrectomy) and to investigate the relationship between the severity of postoperative ANK and retinal microstructures as well as clinical parameters.	Reattached RD Macula-off RD (n= 49) Macula-on RD (n = 57)	n = 106 mean age 56.1 ± 10.9 yrs 68M, 38F FU 6 mos following RD surgery	NAT 45 (42%) ANK 6 mos post-surgery Micropsia: n = 28 (3 w/ M-on, 25 w/M-off) Macropsia: n = 17 (12 w/ M-on, 5 w/ M-off) ANK mag: V ANK: 2.5% ±3.4% H ANK: 2.3% ±2.9% (overall range: -12.5% to 12.0%)	$BCVA_0$: logMAR 0.51 ± 0.76 (20/65)	Approximately ½ of eyes with micropsia had CME, subretinal fluid, and hyper-reflective or disruption of the photoreceptor inner and outer segment junction. More than ½ of eyes with macropsia also exhibited ERM	NR	$BCVA_{6m}$: logMAR 0.04 ± 0.18 (20/22)	Nearly half of patients with successful RD surgery had clinically significant ANK at 6 months follow-up. The amount and type of ANK was associated with best corrected visual acuity and the area of RD. Micropsia was mainly observed in patients with macula-off RD and macropsia mainly observed in patients with macula-on RD.
Lee et al 2014[25] Prospective case series To evaluate the characterization of ANK among patients with successful rhegmatogenous RD following pneumatic retinopexy.	Reattached RD M-on RD n=13 M-off RD n=17	n = 30 mean age 37.6 ± 13 yrs 15M, 15F FU 3, 6, 12 mos	NAT 18 (60%) clinically significant ANK 3 mos post-surgery (15 w/ M-off, 3 w/ M-on) All had micropsia ANK mag: range 1% to 4%	$BCVA_{3,6,12\,m}$: differences between operated and fellow eyes for patients with and without ANK were not significant following surgery	Positive correlation between ANK and difference in central retinal thickness between the operated and unoperated eyes at 3, 6, and 12 mos post-operatively	NR	NR	ANK after pneumatic retinopexy for RD is likely related to the preoperative macular status. Patients with macula-off RD had a higher incidence of ANK postoperatively than patients with macula-on RD (88.2% vs 23.1%).
Chung et al 2015[17] Retrospective case series To identify the relationship between ANK in the vertical and horizontal meridians and the foveal microstructure in patients with unilateral idiopathic ERM.	ERM	n = 65 mean age 63.1 ± 7.9 yrs 19M, 46F FU NR	Computerized NAT 53 (82%) clinically significant ANK All had macropsia V ANK 5.41±5.41% H ANK 4.89±4.83% (overall range 2% to 19%) 25 (47%) had ≥ 2% difference between H and V ANK	$BCVA_0$: log MAR 0.24 ± 0.19 (20/35)	More severe vertical INL thickening correlated with an increased severity of vertical ANK and more severe horizontal INL thickening correlated with an increased severity of horizontal ANK	NR	NR	Most patients with ERM had ANK with macropsia. INL thickness changes may be one of the important etiologies of aniseikonia occurring with ERM. Measurement of ANK in ERM patients should be done on initial examination.
Takabatake et al 2017[18] Prospective observational study To investigate changes and prognostic factors of visual impairment following vitrectomy for unilateral idiopathic ERM.	ERM	n = 45 mean age 64.8 ± 8.6 yrs, 16M, 29F FU 6 & 12 mos	NAT (vertical meridian only) 37 (82%) clinically significant ANK: Macropsia: 36 (80%), Micropsia: 1 (2%) $ANK_{o:}$ 4.9% ± 1.2%	$BCVA_0$: logMAR 0.17 ± 0.05 (20/30) $Metamorphopsia_0$ (quantified using M-CHARTS, Inami Co. Tokyo, Japan) H: 0.77 ± 0.18 V: 0.66 ±0.16	Central foveal thickness, retinal thickness, GCL+ IPL thickness, INL thickness, and ONL + OPL thickness 6 mos and 12 mos after surgery were significantly smaller than at baseline	Surgical	$BCVA_{6m,12m}$: logMAR 0.01+ 0.04 (20/20) $Metamorphopsia_{6m}$: H: 0.33 ± 0.16 V: 0.52 ± 0.16	ANK improved postoperatively with longer follow up (12 versus 6 months) but improvement was slower than both visual acuity and metamorphopsia. More severe ANK and larger horizontal metamorphopsia at baseline were associated with more severe ANK following surgery.

							Metamorphopsia$_{12m}$: H: 0.32 ± 0.15 V: 0.60 ± 0.18 ANK$_{6m}$: 4.4% ± 1.1% ANK$_{12m}$: 3.7% ± 1.0%	
Han et al 2016[19] Prospective single center interventional case series To evaluate changes in ANK in patients with idiopathic unilateral ERM following early surgery.	ERM (mean duration 12.9 ±11.4 mos, range 1 to 38 mos)	n = 24 mean age 64.2 ± 9.3 yrs 11M, 13F FU 6 mos	AI All had ANK with macropsia ANK mag (ave. from 1, 2, 4 and 8^o field angles): V ANK$_o$: 10.6 ± 5.8% (range, 2.5% to 25%) H ANK$_0$: 9.3 ± 6.7% (range, 1% to 25%) ANK greater at smaller visual field angles	BCVA$_o$: logMAR 0.18 ± 0.20 (20/30) Stereopsis: Contour 50" to 800" Global 480" to nil Questionnaire$_0$: documented patient symptoms prior to & 6 mos following surgery Relating to image size differences, distortion, diplopia, and depth perception	Confirmed presence of ERM prior to surgery and its removal following surgery	Surgical	BCVA: 17 pts (71%) had improved VA 6 mos following surgery Mean% age reductions in ANK: V ANK: 41.0% ± 31.4 H ANK 41.6% ± 30.8 Stereo$_{6m}$ improved in 71% contour & 58% global Diplopia$_{6m}$ resolved in 3 of 4 pts	ANK improved following ERM surgery with greater improvement achieved in patients with a shorter duration of symptoms and early surgery, better preoperative BCVA, and when measured at smaller visual field angles. Despite more improvement with earlier surgery, approximately half of preoperative ANK remained in most patients.
Okamoto et al 2016[27] Prospective, interventional case series To quantify the severity of ANK in patients undergoing vitrectomy for idiopathic MH and to examine any relationship between aniseikonia and foveal microstructure.	MH	n = 56 mean age 65.3 ± 5.2 yrs 22M, 34F FU 3, 6, & 12 mos	NAT 35 (62%) had clinically significant aniseikonia Micropsia: 31 (55%) Macropsia: 4 (7%), ANK$_o$: -3.2 ± 4.6% (range -15.5 to 5%)	BCVA$_o$: logMAR 0.72 ± 0.33 (20/105)	Preoperative ANK correlated significantly with minimum and base diameter of MH and defect length of ELM Post-op ANK not associated with any pre-op OCT parameter	Surgical	BCVA$_{12m}$: logMAR 0.20±0.21 (20/32) ANK$_{3m}$: -1.2 ± 1.8% ANK$_{12m}$: -1.0 ± 1.5%	Approximately half of patients with idiopathic macular hole had aniseikonia with micropsia which improved following surgery. Severity of preoperative aniseikonia was associated with macular hole size and ELM status.
Sugiura et al 2016[32] and **Ofusa et al 2014**[33] Two Prospective case series To evaluate ANK and other visual functions in patients with unilateral IMT type 1, compare to findings in age-matched controls, and determine the effect of intravitreal bevacizumab on these visual functions	IMT type 1	n = 18 mean age 68.1 ± 4.8 yrs 11M, 7F FU 1 month	NAT All had ANK All had micropsia ANK$_o$: -2.7 ±3.1% (range, -9.0 to 0)	BCVA: logMAR 0.23 ± 0.28 (20/34) All visual functions were significantly worse compared to matched controls: Metamorphopsia (M-Charts), Contrast sensitivity (CSV – 1000E chart), stereopsis (Titmus and TNO stereotests)	Central foveal thickness: IMT type 1 395 ± 69um, Controls 159± 24 um	Intravitreal Bevacizumab (n = 7)	Improvement after 1 month for all visual functions except stereopsis BCVA: n=6 (86%) ANK: n=5 (71%) Contrast sensitivity: n=5 (71%) Metamorphopsia: n=4 (57%)	In addition to reduced BCVA, IMT type 1 causes ANK with micropsia and significantly affects metamorphopsia, contrast sensitivity, and stereopsis. Intravitreal bevacizumab can improve ANK and most other visual functions.
Okamoto et al 2017[20] Prospective case series To quantify and compare the severity of ANK in patients undergoing vitrectomy for various retinal disorders.	ERM (n = 81) MH (n = 80) ME (n = 60) BRVO-CME, CRVO-CME, DME Re-attached RD (n = 136) M-on & M-off Control group (n =31)	n = 357 mean age 62.3 ± 11.0 yrs 204 M, 153 F FU 6 mos	NAT 131 of 221 (59%) had ANK* Overall ANK$_o$: 4.0 ± 4.1% (range -21.5% to 19.5%) ANK ERM$_0$: 5.1 ± 4.4%, (macropsia 68%) ANK MH$_0$: 3.3 ± 3.8% (micropsia 48%) ANK BRVO-CME$_0$: 3.3 ± 3.6% (micropsia 39%) ANK CRVO-CME$_0$: 4.4% ± 5.9% (micropsia 50%) ANK DME$_0$: 2.5 ± 2.2% (micropsia 45%) *ANK was not measured preoperatively for M-off RD and M-on RD	BCVA (overall)$_0$: logMAR 0.46 ±0.55 (20/58)	Macropsia with ERM can be offset by micropsia due to coexisting CME or subretinal fluid	Surgical	BCVA overall$_{6m}$: logMAR 0.18±0.28 (20/30) ANK overall$_{6m}$: 3.0 ± 3.6% (range -20.5% to 17%) ANK ERM$_{6m}$: 5.0 ± 4.4% (macropsia 69%) ANK MH$_{6m}$: 1.7 ± 2.1% (micropsia 18%) ANK BRVO-CME$_{6m}$: 2.9 ± 3.0% (micropsia 48%) ANK CRVO-CME$_{6m}$ 5.3 ± 6.3% (micropsia 60%) ANK DME$_{6m}$: 3.0 ± 3.3% (micropsia 45%) ANK M–off RD*: 3.3 ± 3.4% (micropsia 48%) ANK M–on RD*: 1.3 ± 2.1% (75% had no ANK)	More than half of patients with various retinal disorders had ANK, its amount being more severe with ERM. Macropsia was dominant with ERM whereas micropsia was more conspicuous with the other retinal disorders. Surgery significantly improved best corrected visual acuity in all conditions except CRVO-CME whereas ANK improved only in MH. With most retinal disorders, even after successful surgery and improvement in best corrected visual acuity, abnormal distribution of photoreceptors cannot be restored and clinically significant amounts of ANK remain.
Ichikawa et al 2018[21] Retrospective case series To determine the correlation of the degree of ANK with the retinal displacement and metamorphopsia in patients who have undergone successful ERM surgery 3 months earlier.	ERM	n = 28 mean age 68.3 ± 7.1 yrs 11M,17F FU 3 mos	NAT (vertical meridian only) 20 had clinically significant ANK (71%) All had macropsia ANK$_o$: 3.72±3.71% (range 1 to 15%)	BCVA: logMAR 0.23 ± 0.13 (20/34) Metamorphopsia (M - CHARTS): Vert 0.56 ± 0.60 Hor 0.82 ± 0.74	Severity of both ANK and metamorphopsia was significantly correlated with tangential retinal contraction	Surgical	BCVA$_{3m}$: logMAR 0.04 ± 0.13 (20/22) Metamorphopsia improved significantly only in the horizontal meridian: Metamorphopsia: H$_{3m}$ 0.43 ± 0.50 ANK$_{3m}$: 3.6%	Preoperative and postoperative ANK were significantly correlated with preoperative and postoperative Metamorphopsia and with the ratio of the tangential retinal displacements after surgical removal of ERM. ANK is less likely than metamorphopsia to recover following ERM surgery.
Tanikawa, et al 2018[22] Prospective case series To compare best corrected visual acuity, metamorphopsia, and ANK in patients with unilateral, idiopathic ERM.	ERM	n = 61 mean age 62.1 ± 8.1 29M,32F FU NR	NAT (vertical meridian only) 46 had ANK (75%) All had macropsia ANK$_0$ range 1 to 14%	BCVA (median): logMAR 0.15 (20/28) ANK with normal BCVA n=12 ANK with metamorphopsia n=23 ANK without metamorphopsia n=6 Metamorphopsia without ANK n=11	Confirmed diagnosis of ERM	NR	NR	The magnitudes of ANK and metamorphopsia were not significantly correlated with each other or with best corrected visual acuity in patients with ERM. In addition to visual acuity, quantitative testing for ANK and metamorphopsia are necessary to assess visual function in patients with ERM.

ANK = aniseikonia (ANK$_o$ = baseline, ANK$_{3m}$ = 3 mos, ANK$_{6m}$ = 6 mos, ANK$_{12m}$ = 12 mos), V ANK = vertical aniseikonia, H ANK = horizontal aniseikonia, H = horizontal, V = vertical, BCVA = best corrected visual acuity in affected eye (BCVA$_o$, baseline, BCVA$_{3m}$, 3 months, BCVA$_{6m}$., 6 months), NAT = New Aniseikonia Test, AI = Aniseikonia Inspector, OCT = optical coherence tomography, FU = follow up, NR = not reported, ERM = epiretinal membrane, RD = retinal detachment, M-on RD = macula on retinal detachment, M-off RD = macula off retinal detachment, MH = macular hole, ME = macular edema, CME = cystoid macular edema, BRVO - CME = cystoid macular edema with branch venous occlusion, CRVO-CME = cystoid macular edema with central venous occlusion, DME = diabetic macular edema, IMT = idiopathic macular telangiectasia, ARMD = age related macular degeneration, INL = inner nuclear layer, ONL = outer nuclear layer, ELM = external limiting membrane, IS/OS line = photoreceptor inner and outer segment junction, GCL = ganglion cell layer, OPL = outer plexiform layer
# mean values unless specified otherwise