

Ellipsoid Zone

Area Loss: An Independent Predictor of Reduced Fixation Stability in Patients With Macular Telangiectasia Type 2

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Purpose

To determine whether EZ area loss independently predicts fixation stability in individuals with MacTel

Conclusions

EZ area loss is an important, independent predictor of reduced fixation stability in MacTel

An EZ area loss of approximately 1 mm² represents a clinically meaningful threshold above which patients are at high risk for fixation instability, supporting the utility of EZ area quantification as a surrogate biomarker for visual function in MacTel

References

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Disclosures

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Background

- Individuals with macular telangiectasia type 2 (MacTel) may have near-normal best-corrected visual acuity despite experiencing reduced reading speeds and metamorphopsia¹
- Reduced fixation stability has been found in patients with MacTel and is associated with reduced reading speed²
- Evaluation of fixation stability on microperimetry testing may serve as an important clinical tool in assessing disease progression in MacTel^{2,3}

Methods

- This observational longitudinal analysis used ellipsoid zone (EZ) data from two Phase 3 trials of revakinagene taroretcel-lwey for MacTel⁴
- EZ area loss was quantified using en face optical coherence tomography⁴
- Fixation stability was measured by microperimetry and quantified using the P1 fixation stability index (percentage of fixation points within a 1° diameter circle)⁵
- Multiple linear regression assessed the association between EZ area loss and P1 fixation stability at baseline and Month 24, adjusting for age and fixation losses
- Multivariate logistic regression evaluated predictors of poor fixation stability
- Linear mixed-effects model (LMM) evaluated longitudinal trends by estimating fixation loss percentage at baseline and Month 24
 - Covariates included visit, baseline EZ area loss, and the interaction between these two effects
 - A patient-specific random effect was also included
- Receiver operating characteristic (ROC) analysis was performed to establish a structural threshold for poor fixation stability

Results

Study Population

- Of 228 enrolled patients, 212 had complete longitudinal EZ and microperimetry data

Table 1. Baseline Demographics and Clinical Characteristics

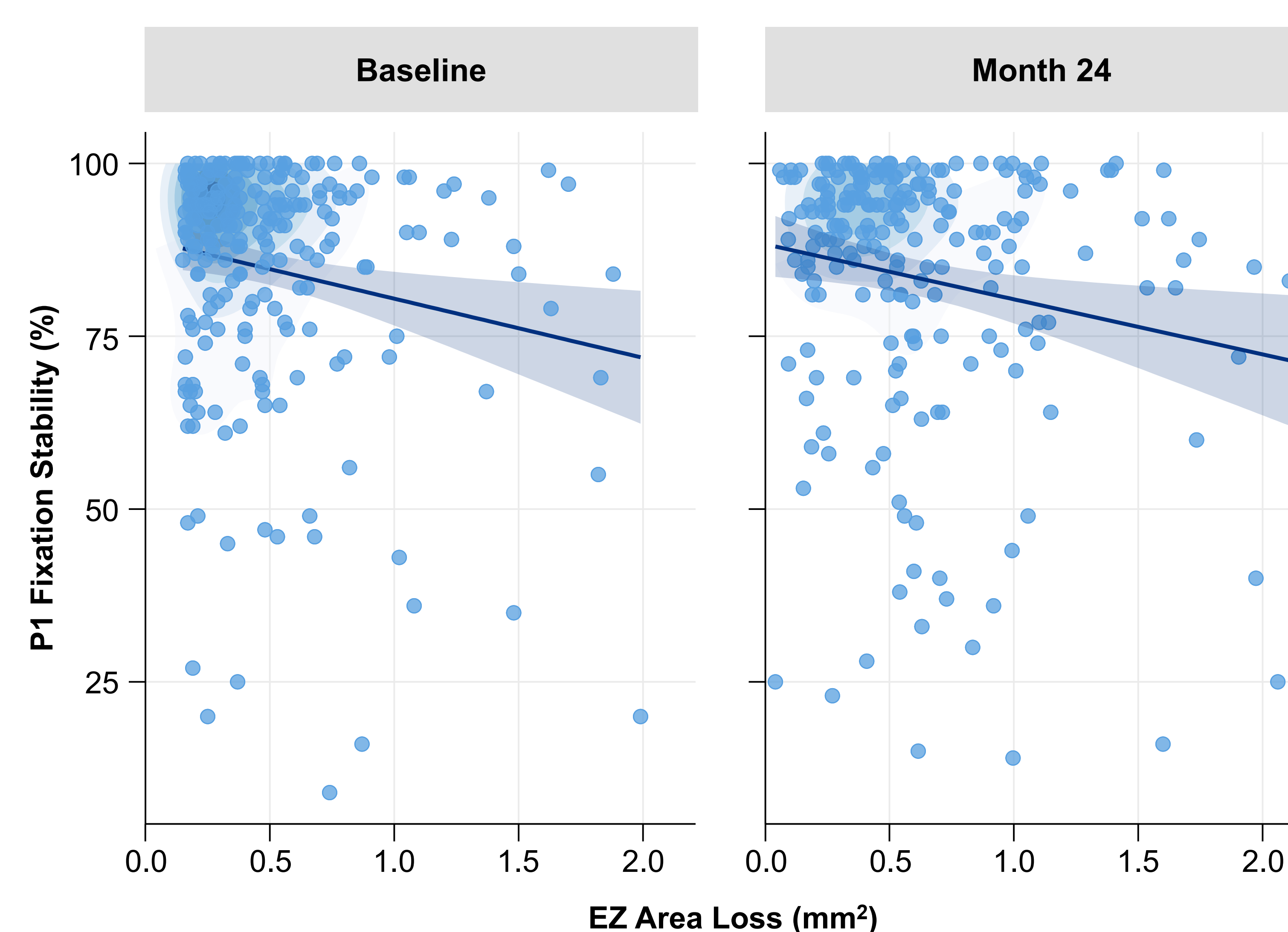
Variable	Overall (N=212)	Low EZ Area Loss (n=106)	High EZ Area Loss (n=106)
Age, mean±SD, years	59.6±8.2	59.7±8.3	59.3±8.0
Female, %	70.3	64.2	76.2
Eye laterality, OD/OS, n/n	92/120	48/58	44/62
Baseline EZ area loss, mean±SD, mm ²	0.49±0.37	0.25±0.07	0.73±0.38
Baseline P1 fixation stability, median (IQR), %	91 (18)	93 (11)	89 (20)

High EZ area loss was defined as ≥0.38 mm²; low EZ area loss was defined as <0.38 mm². EZ, ellipsoid zone; IQR, interquartile range; OD, oculus dexter (right eye); OS, oculus sinister (left eye); SD, standard deviation.

EZ Area Loss as an Independent Predictor of P1 Fixation Stability

- EZ area loss was negatively associated with P1 fixation stability at baseline ($\beta=-9.43$; $P=0.002$) and at Month 24 ($\beta=-7.89$; $P=0.01$)
- Heat maps (Figure 1) highlight the high-concentration “core” of the patient population, demonstrating a clear downward trend in fixation stability as EZ area loss increases
 - This visualization emphasizes the primary biological signal while accounting for the high degree of clinical variability inherent in microperimetry
- At Month 24, each 1-mm² increase in EZ area loss doubled the odds of poor fixation stability (odds ratio, ≈2.0; $P=0.047$)

Figure 1. Density mapping of structure–function relationship

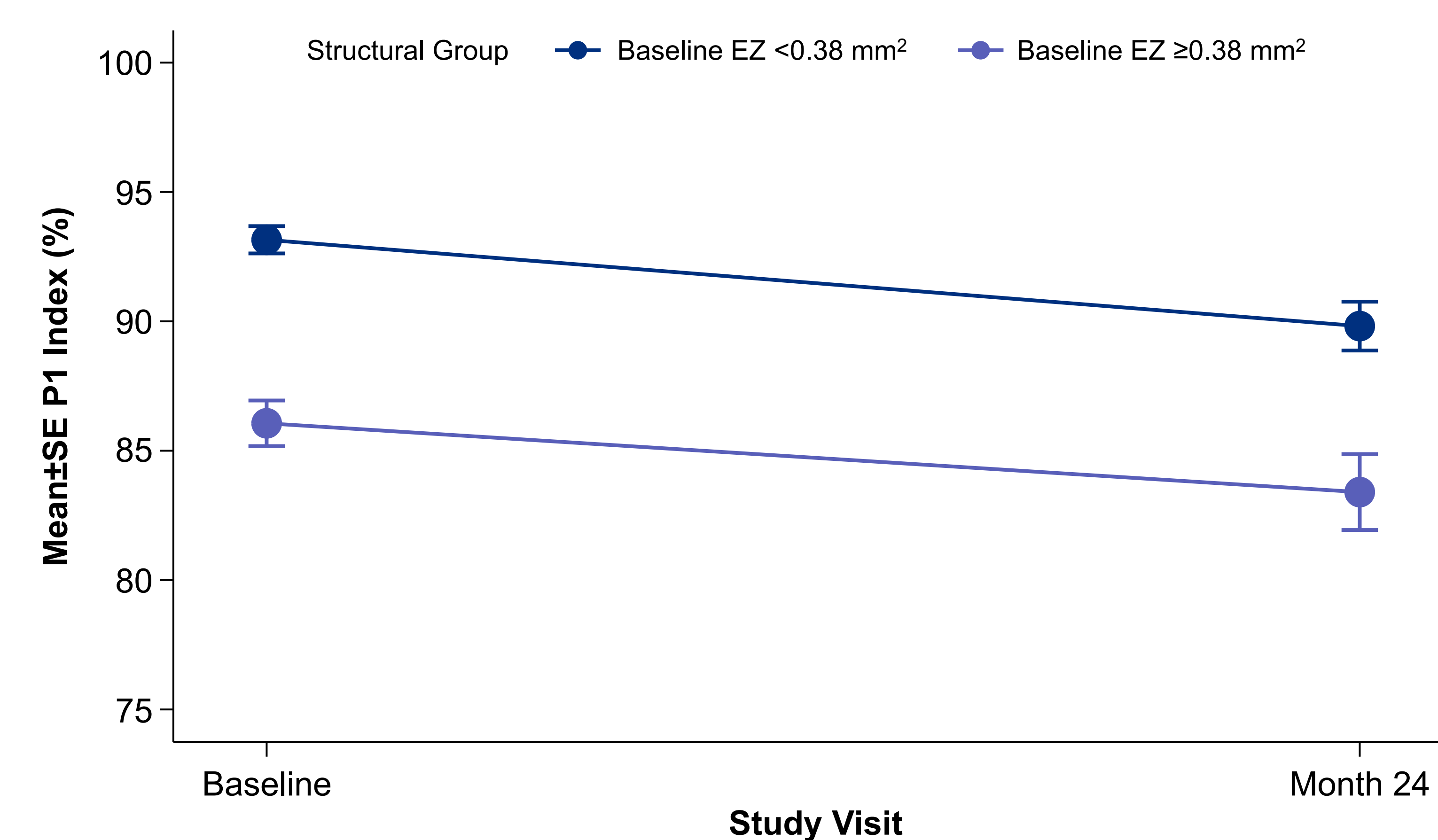


This scatterplot shows the relationship between EZ area loss (mm²) and P1 fixation stability (%) at baseline and Month 24. The regression line (solid) and 95% confidence intervals (shaded) illustrate the significant decline in fixation stability as EZ area loss increases. EZ, ellipsoid zone.

Longitudinal Fixation Stability

- In the LMM, eyes with EZ area lesion size greater than or equal to the median loss at baseline showed a numerically lower fixation stability percentage at 24 months compared to those with less than the median loss, but this difference was not statistically significant ($P=0.084$) (Figure 2)
 - There was no significant difference in fixation stability percentage between the two groups at baseline ($P=0.23$)
 - The interaction between visit and baseline EZ area loss was not statistically significant ($P=0.68$)

Figure 2. Longitudinal fixation stability by baseline EZ area loss group

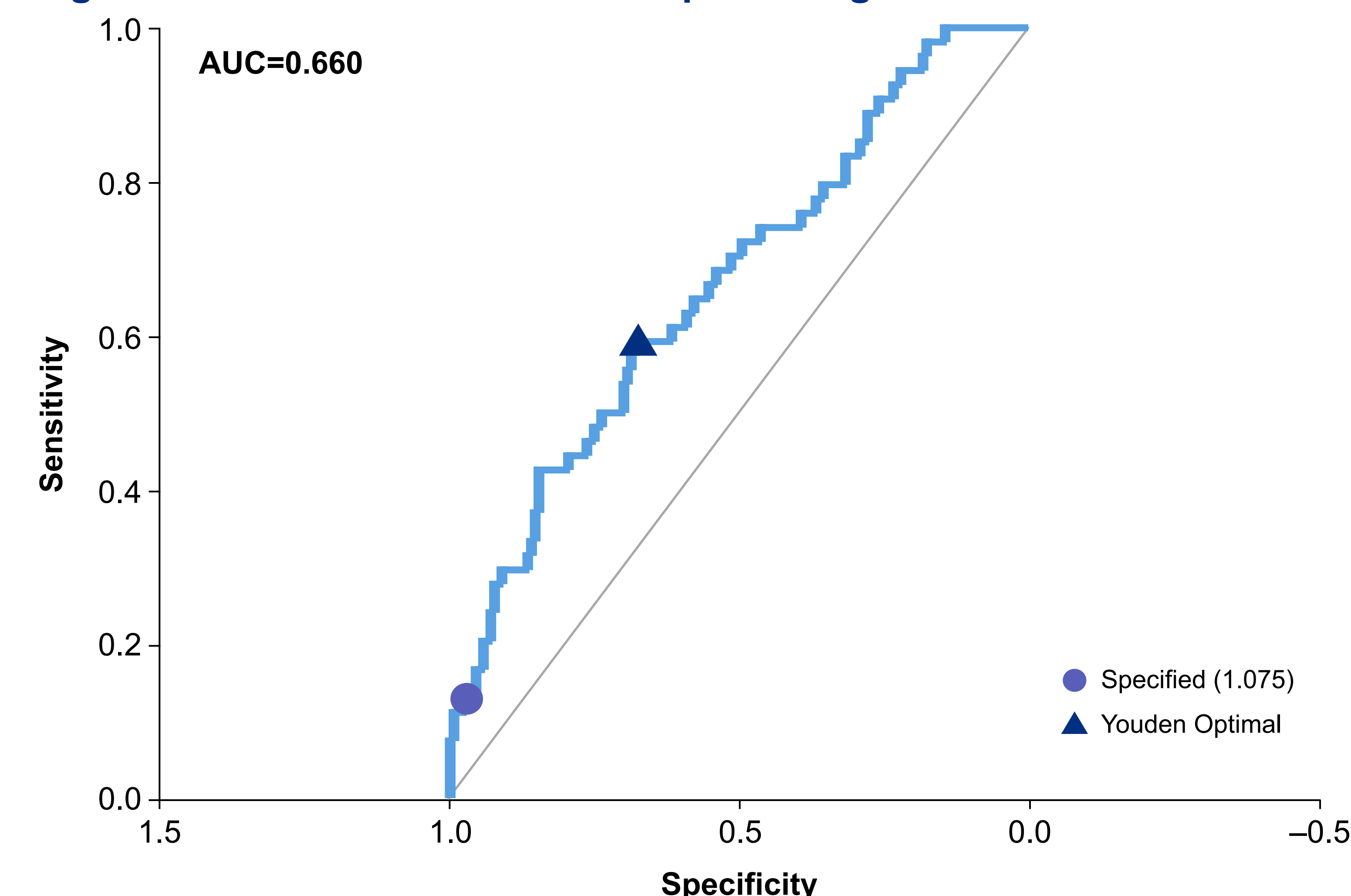


The line graph displays the mean P1 index (percentage) at baseline and 24 months for two treatment cohorts: those with low baseline EZ area loss (<0.38 mm²; blue line) and those with high baseline EZ area loss (≥0.38 mm²; purple line). Error bars represent the SE. EZ, ellipsoid zone; SE, standard error.

ROC Threshold Analysis

- The ROC analysis identified a threshold of 1.075 mm² of EZ area loss for predicting unstable fixation (Figure 3)
 - AUC was 0.660, which represents moderate discriminative ability

Figure 3. ROC curve: EZ area loss predicting unstable fixation



The ROC curve for EZ area loss is a predictor of unstable fixation. The ROC curve (light blue line) illustrates the diagnostic ability of EZ area loss to discriminate between participants who did develop unstable fixation versus those who did not over the 24 months. The AUC is 0.660, indicating a modest predictive value. The blue triangle represents the Youden Optimal cutoff points, which maximize the sum of sensitivity and specificity. The purple circle indicates a threshold of 1.075 mm². The diagonal grey line represents the line of identity (AUC=0.50), corresponding to the predictor with no better than random chance performance. AUC, area under the curve; EZ, ellipsoid zone; ROC, receiver operating characteristic.