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**Authors:** Constantin Geis, Márta Germán-Salló, Beáta Baróti, Tünde Pál, Zoltán Preg, Enikő Nemes-Nagy, Henrik Haba, Lajos Csincsik and Robert G. Tripon

**Corresponding author:** Constantin Geis

**Affiliation:** Department of Ophthalmology - George Emil Palade University of Medicine, Pharmacy, Science, and Technology of Targu Mures, Targu Mures, Romania

**E-mail:** constantingeis@gmail.com

### Online Resource 3: Complete GEE Model analyses

#### Complete GEE Model analyses of non-significant and significant results (\*P < 0.05 indicates statistical significance)

| VDa          | Estimate | Std. Error | 95% CI Lower | 95% CI Upper | P-Value  |
|--------------|----------|------------|--------------|--------------|----------|
| (Intercept)  | 0.03     | 0.009      | 0.01         | 0.04         | 0.001*   |
| TML size (%) | -0.0004  | 0.0001     | -0.0006      | -0.0002      | < 0.001* |
| Age          | 0.00003  | 0.0001     | -0.0002      | 0.0003       | 0.79     |
| Sex          | 0.003    | 0.001      | -0.00004     | 0.006        | 0.053    |

Table 6: GEE Model Results – VDa

Generalized estimating equation model with TML size (%) as predictor and VDa as outcome variable, including age and sex as covariates. Abbreviations: VDa, artery vessel density; TML, Thalamic Microvascular Lesion size; CI, Confidence Interval.

| Artery Average Width | Estimate | Std. Error | 95% CI Lower | 95% CI Upper | P-Value  |
|----------------------|----------|------------|--------------|--------------|----------|
| (Intercept)          | 82.56    | 16.02      | 51.15        | 113.96       | < 0.001* |
| TML size (%)         | -0.19    | 0.18       | -0.55        | 0.16         | 0.27     |
| Age                  | 0.08     | 0.23       | -0.37        | 0.53         | 0.72     |
| Sex                  | 3.30     | 1.96       | -0.54        | 7.14         | 0.09     |

Table 7: GEE Model Results – Artery Average Width

Generalized estimating equation model with TML size (%) as predictor and artery average width as outcome variable, including age and sex as covariates.

| <b>Artery Distance Tortuosity</b> | <b>Estimate</b> | <b>Std. Error</b> | <b>95% CI Lower</b> | <b>95% CI Upper</b> | <b>P-Value</b> |
|-----------------------------------|-----------------|-------------------|---------------------|---------------------|----------------|
| (Intercept)                       | -3.19           | 7.88              | -18.65              | 12.26               | 0.68           |
| TML size (%)                      | -0.05           | 0.09              | -0.24               | 0.12                | 0.52           |
| Age                               | 0.12            | 0.11              | -0.09               | 0.34                | 0.25           |
| Sex                               | 0.32            | 1.08              | -1.79               | 2.44                | 0.76           |

Table 8: GEE Model Results – Artery Distance Tortuosity

Generalized estimating equation model with TML size (%) as predictor and artery distance tortuosity as outcome variable, including age and sex as covariates.

| <b>VDv</b>   | <b>Estimate</b> | <b>Std. Error</b> | <b>95% CI Lower</b> | <b>95% CI Upper</b> | <b>P-Value</b> |
|--------------|-----------------|-------------------|---------------------|---------------------|----------------|
| (Intercept)  | 0.04            | 0.014             | 0.019               | 0.07                | < 0.001*       |
| TML size (%) | -0.0001         | 0.0001            | -0.0003             | 0.0001              | 0.47           |
| Age          | -0.0001         | 0.0002            | -0.0006             | 0.0002              | 0.45           |
| Sex          | 0.001           | 0.001             | -0.002              | 0.004               | 0.53           |

Table 9: GEE Model Results – VDv

Generalized estimating equation model with TML size (%) as predictor and VDv as outcome variable, including age and sex as covariates. Abbreviations: VDv, vein vessel density.

| <b>Vein Average Width</b> | <b>Estimate</b> | <b>Std. Error</b> | <b>95% CI Lower</b> | <b>95% CI Upper</b> | <b>P-Value</b> |
|---------------------------|-----------------|-------------------|---------------------|---------------------|----------------|
| (Intercept)               | 110.53          | 16.28             | 78.61               | 142.46              | < 0.001*       |
| TML size (%)              | 0.01            | 0.24              | -0.45               | 0.49                | 0.93           |
| Age                       | -0.13           | 0.24              | -0.62               | 0.34                | 0.57           |
| Sex                       | 6.73            | 2.49              | 1.84                | 11.63               | 0.006*         |

Table 10: GEE Model Results – Vein Average Width

Generalized estimating equation model with TML size (%) as predictor and Vein Average Width as outcome variable, including age and sex as covariates.

| <b>Vein Distance Tortuosity</b> | <b>Estimate</b> | <b>Std. Error</b> | <b>95% CI Lower</b> | <b>95% CI Upper</b> | <b>P-Value</b> |
|---------------------------------|-----------------|-------------------|---------------------|---------------------|----------------|
| (Intercept)                     | -8.44           | 7.24              | -22.64              | 5.76                | 0.24           |

|              |       |      |       |      |      |
|--------------|-------|------|-------|------|------|
| TML size (%) | -0.11 | 0.07 | -0.25 | 0.02 | 0.11 |
| Age          | 0.20  | 0.10 | -0.01 | 0.41 | 0.06 |
| Sex          | -0.03 | 0.93 | -1.86 | 1.78 | 0.96 |

Table 11: GEE Model Results – Vein Distance Tortuosity

Generalized estimating equation model with TML size (%) as predictor and Vein Distance Tortuosity as outcome variable, including age and sex as covariates.

| <b>CRVE Hubbard Zone B</b> | <b>Estimate</b> | <b>Std. Error</b> | <b>95% CI Lower</b> | <b>95% CI Upper</b> | <b>P-Value</b> |
|----------------------------|-----------------|-------------------|---------------------|---------------------|----------------|
| (Intercept)                | 369.95          | 104.96            | 164.21              | 575.69              | < 0.001*       |
| TML size (%)               | 0.92            | 1.08              | -1.20               | 3.05                | 0.39           |
| Age                        | -1.19           | 1.59              | -4.32               | 1.92                | 0.45           |
| Sex                        | 16.76           | 11.18             | -5.15               | 38.67               | 0.13           |

Table 12: GEE Model Results – CRVE Hubbard Zone B

Generalized estimating equation model with TML size (%) as predictor and CRVE Hubbard Zone B as outcome variable, including age and sex as covariates. Abbreviations: CRVE, Central Retinal Venular Equivalent.

| <b>CRVE Hubbard Zone C</b> | <b>Estimate</b> | <b>Std. Error</b> | <b>95% CI Lower</b> | <b>95% CI Upper</b> | <b>P-Value</b> |
|----------------------------|-----------------|-------------------|---------------------|---------------------|----------------|
| (Intercept)                | 479.83          | 102.36            | 279.20              | 680.46              | < 0.001*       |
| TML size (%)               | 1.55            | 0.88              | -0.18               | 3.29                | 0.079          |
| Age                        | -2.48           | 1.50              | -5.43               | 0.46                | 0.09           |
| Sex                        | 24.57           | 11.23             | 2.56                | 46.59               | 0.02*          |

Table 13: GEE Model Results – CRVE Hubbard Zone C

Generalized estimating equation model with TML size (%) as predictor and CRVE Hubbard Zone C as outcome variable, including age and sex as covariates.

| <b>FD</b>    | <b>Estimate</b> | <b>Std. Error</b> | <b>95% CI Lower</b> | <b>95% CI Upper</b> | <b>P-Value</b> |
|--------------|-----------------|-------------------|---------------------|---------------------|----------------|
| (Intercept)  | 1.51            | 0.05              | 1.40                | 1.63                | < 0.001*       |
| TML size (%) | -0.001          | 0.0006            | -0.002              | -0.0003             | 0.012*         |
| Age          | -0.0004         | 0.0008            | -0.002              | 0.001               | 0.62           |

|     |       |       |       |      |      |
|-----|-------|-------|-------|------|------|
| Sex | 0.005 | 0.009 | -0.01 | 0.02 | 0.53 |
|-----|-------|-------|-------|------|------|

Table 14: GEE Model Results – FD

Generalized estimating equation model with TML size (%) as predictor and FD as outcome variable, including age and sex as covariates. Abbreviations: FD, Fractal Dimension.

| <b>CRAE Zone B</b>        | <b>Estimate</b> | <b>Std. Error</b> | <b>95% CI Lower</b> | <b>95% CI Upper</b> | <b>P-Value</b> |
|---------------------------|-----------------|-------------------|---------------------|---------------------|----------------|
| (Intercept)               | 262.69          | 55.01             | 154.86              | 370.52              | < 0.001*       |
| TML size (%)              | -1.266          | 0.61              | -2.47               | -0.05               | 0.040*         |
| Age                       | -0.452          | 0.77              | -1.97               | 1.07                | 0.561          |
| Sex<br>(Male=1, Female=0) | 16.523          | 8.16              | 0.51                | 32.53               | 0.043*         |

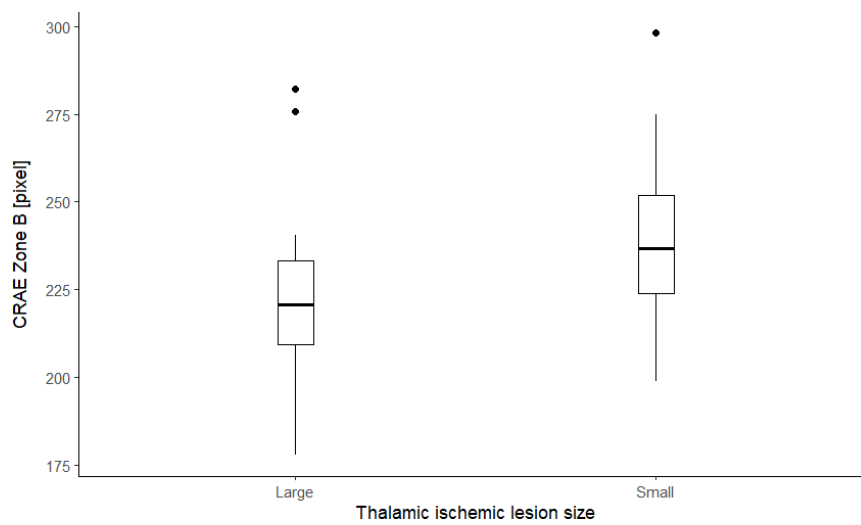
Table 15: GEE Model Results – CRAE Zone B

Generalized estimating equation model with TML size (%) as predictor and CRAE Zone B as outcome variable, including age and sex as covariates. Abbreviations: CRAE, Central Retinal Arteriolar Equivalent.

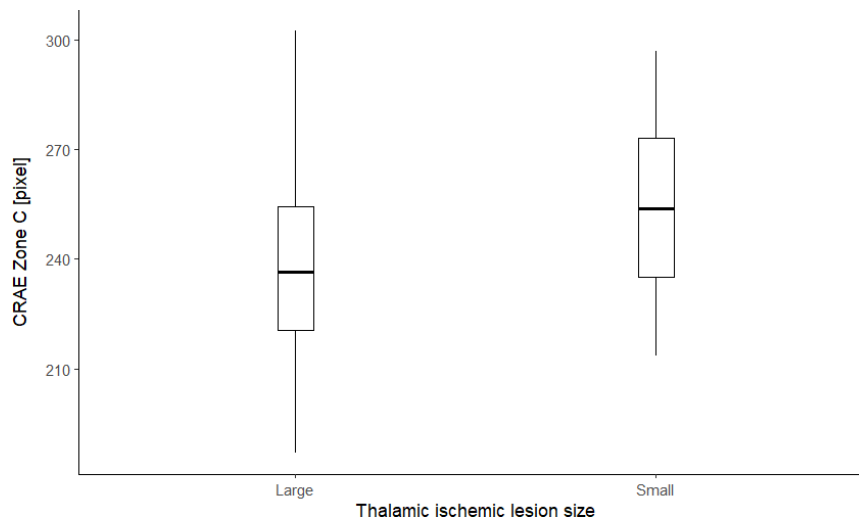
| <b>CRAE Zone C</b>        | <b>Estimate</b> | <b>Std. Error</b> | <b>95% CI Lower</b> | <b>95% CI Upper</b> | <b>P-Value</b> |
|---------------------------|-----------------|-------------------|---------------------|---------------------|----------------|
| (Intercept)               | 254.98          | 61.33             | 134.76              | 375.19              | < 0.001*       |
| TML size (%)              | -1.236          | 0.62              | -2.46               | -0.009              | 0.048*         |
| Age                       | -0.141          | 0.88              | -1.87               | 1.59                | 0.874          |
| Sex<br>(Male=1, Female=0) | 18.192          | 9.17              | 0.20                | 36.17               | 0.047*         |

Table 16: GEE Model Results – CRAE Zone C

Generalized estimating equation model with TML size (%) as predictor and CRAE Zone C as outcome variable, including age and sex as covariates. Abbreviations: CRAE, Central Retinal Arteriolar Equivalent.



Graph 1: Boxplot, representing TML size (%) categorized according to the median of all measurements into large (above median) and small (below median). The y-axis depicts CRAE in Zone B [pixel].



Graph 2: Boxplot, representing TML size (%) categorized according to the median of all measurements into large (above median) and small (below median). The y-axis depicts CRAE in Zone C [pixel].