USING BOX-COUNTING DIMENSION TO CHARACTERIZE DIFFERENT STAGES OF DIABETIC RETINOPATHY

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Mathematics

A. Rationale:

Self-similar fractal patterns in the human body exhibit quantifiable characteristics regarding their orientation and/or complexity. One such example is fractal dimension, which *"can be used as a measure for morphological complexity in biological systems* (Koschutnig, Enzinger, Franz Ebner, Helmut Ahammer, *2012*)." These biological systems include lung bronchioles, blood vessels, cancerous and benign tumors, abnormal lesions, etc. Many afflictions are characterized by a fractal-like growth, and fractal analysis (including the box-counting method) is an emerging method used to quantify these patterns.

Studies of retinal vessels (which exhibit self-similarity) using fractal analysis have been made previously, including the effect of various diseases, one example being CADASIL, on box-counting dimension. One such disease that has yet to be investigated is diabetic retinopathy, a side-effect of type-II diabetes that affects the retina; it is characterized by microaneurysms, hard and soft exudates, hemorrhages, and in some cases, neovascularization (the abnormal growth of new vessels). The presence of neovascularization indicates the diabetic retinopathy is proliferative, as opposed to non-proliferative.

B. Research Questions / Hypotheses:

Do retinal vessels with diabetic retinopathy exhibit a significant difference in box-counting dimension compared to retinal vessels unaffected by diabetic retinopathy? Do retinal vessels

with neovascularization exhibit a significant increase in box-counting dimension than those in the nonproliferative groups?

H_o : There is no significant difference between the fractal dimensions of retinal vessels affected by diabetic retinopathy and the control group.

H_A : There is a significant difference between the fractal dimensions of retinal vessels affected by diabetic retinopathy and the control group.

H_o : There is a significant increase between the fractal dimensions of the retinal vessels exhibiting neovascularization.

H_A : There is no significant increase in the fractal dimensions of retinal vessels exhibiting neovascularization.

C. Methodology and Data Analysis:

1) Medical images of retinal vessels will be obtained from the *DIARETDB0 Diabetic Retinopathy Databas*e, with the the images being separated into a control group and four test groups with diabetic retinopathy, representing the stages of the disease. The first two stages are non-proliferative and the last two are proliferative.

2) Using ImageJ, regions of interest (ROI) will be isolated, grayscaled, and binarized to be processed by the ImageJ plugin FracLac.
3) FracLac will compute the mean box-counting dimensions, which are calculated as an average of the dimensions across different regions. The default settings will be used.
4) Multiple images from each group will be analyzed to compute precise data averages, and all data will be recorded.

FracLac will automatically apply boxes over several magnifications, computing twelve different values and obtaining an average: the mean box-counting dimension. The fractal dimension of the retinal vessels in the control group will be compared to those of the test group. In addition, the two groups exhibiting neovascularization will be compared to the three groups that don't exhibit neovascularization. The significance of the results will be computed using a t-test, with $p < 0.05$ being considered statistically significant and $p < 0.01$ being considered highly significant. The ANOVA test will be used to determine a significant difference between any of the five groups. Several trials will be completed.

D. Bibliography:

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