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chamber angle configuration demands considering at least three separate characteristics: the locus of the attachment of the iris to the inner wall of the eye (the ciliary body, the angle recess, or the cornea), the curvature of the peripheral iris, and the space between the iris and the cornea as measured with diametry, or anterior chamber depth or estimate of angularity as in the Shaffer system. No one has yet figured out a way to put these three variables together in a meaningful way. Even more seriously misleading, however, is the practice of ignoring one or more of the variables. Consequently, the results of various studies are literally comparing 'apples' and 'oranges' so it is not surprising that there is so much disagreement amongst these. For example, UBM is a beautiful way to evaluate two aspects of configuration, specifically the curvature of the iris, and the 'angularity'. However, because the site of the posterior trabecular meshwork is not well defined in UBM and because the relationship of the posterior trabecular meshwork with the insertion of the iris varies markedly, UBM is not a good method of characterizing the entire nature of the anterior chamber angle, or explaining why patients are likely to develop angle closure. He and colleagues' article points out some of these shortcomings and moves the field ahead. However, what is still missing is a unifying description that recognizes that configuration requires incorporating various variables.

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Sir, Reply to Dr Spaeth

We would like to thank Dr Spaeth for his kind comments and heartily agree with him that iridotrabecular angle is but one of a myriad of anatomical characteristics of the iridotrabecular recess that is likely to determine risk of contact between iris and trabecular meshwork. However, it is one with a proven association between evidence of anterior segment pathology (PAS) and glaucomatous optic neuropathy.¹ Dr Spaeth's classification identifying iridotrabecular angle, iris profile, as well as the apparent and true level of iris insertion is currently unsurpassed for describing gonioscopic anatomy in cases of angle-closure.² However, the advent of UBM and OCT imaging of anterior segment structures has helped reinforce our awareness that the relationship of iris and trabecular meshwork change on a second to second basis.³ The ultimate challenge will be to assimilate the static features that Spaeth highlights into a comprehensive, dynamic model of the determinants of iridotrabecular contact, which is validated in longitudinal studies of incident angle-closure and glaucomatous optic neuropathy.

References

- 1 Foster PJ, Nolan WP, Aung T, Machin D, Baasanhu J, Khaw PT *et al.* The definition of an 'occludable' angle: drainage angle width, peripheral anterior synechiae and glaucomatous optic neuropathy in East Asian people. *Br J Ophthalmol* 2004; **88**: 486–490.
- 2 Spaeth GL. The normal development of the human anterior chamber angle: a new system of descriptive grading. *Trans Ophthalmol Soc UK* 1971; **91**: 709–739.
- 3 Gazzard G, Foster PJ, Friedman DS, Khaw PT, Seah S. Light to dark physiological variation in irido-trabecular angle width. *Br J Ophthalmol* 2000 (Peer reviewed video report http://bjo.bmjjournals.com/cgi/content/full/88/11/DC1/1).

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Sir,

On eye analyses

The articles by Halberstadt *et al*,¹ Taner *et al*,² and Loukovaara *et al*³ illustrate systemic errors in statistical analysis. They use two-sample *t*-tests or analysis of variance (ANOVA), but ignore their shortcomings. These compare the means of normal populations assuming unknown homogeneous variances. While the Central Limit Theorem justifies normality for inferences on means, unknown variances need not be equal, making these tests unsuitable for general mean comparisons. As the joint distribution of sample means of normal populations is a function of the ratio of their unknown variances, tests based on the difference between sample means of normal populations with unknown unequal variances are inexact, and not a *t*-test.⁴

This problem is not removed by meaninglessly⁵ testing for the equality of variances, or avoiding normality with its nuisance unknown variances with nonparametric rank tests such as the Wilcoxon test. Being a comparison of distributions, these rank tests say nothing specifically about the mean, median, or any moment of the distributions if significant. They are moreover biased⁶ to one side in a two-sided test.

Tsakok⁷ has solved this Behrens–Fisher problem of comparing the means of normal distributions with unknown variances at exact significance levels, showing that the Tsakok solution is more effective in detecting significant mean differences even with unknown equal variances. There is an indication⁸ that the Tsakok technique applies to dependent samples. Its exposition⁹ is available.

The software GSP implements the Tsakok technique. It is now used for mean comparisons at 0.02 significance level (one significant figure) per pair.

Unfortunately, it is not possible to apply GSP to the article by Loukovaara *et al*³ because, ignoring baseline characteristics, they did not publish the sufficient statistics for ANOVA (sample means and standard deviations), obstructing the minimum requirement of facilitating independent verification.

For Table 3,¹ there are significant mean differences between phakic and pseudophakic patients in their total number of breaks (preoperative and intraoperative), bestcorrected visual acuity (BCVA) 6 months after scleral buckling and BCVA 6 months after vitrectomy.

For Table 2,² there is a significant mean difference between basal and after cyclopentolate for the resistive index (RI) of pseudoexfoliation syndrome (PXS).

There is little or no overlap, well below 95% with at least population, between the 99% confidence intervals of the clinical groups concerned.

The care taken with the data means that they deserve correct analysis, which they were denied.

The Tsakok technique is extended to the nonparametric problem of comparing samples using the article on constructing exact unconditional Uniformly Most Powerful Unbiased tests by Tsakok,¹⁰ superseding the χ^2 test or the Wilcoxon test. The Tsakok articles are reprinted¹¹ with further results.

References

reattachment surgery: anatomical and functional outcome in phakic and pseudophakic eyes. *Eye* 2005; **19**: 891–898.

- 2 Taner P, Unal B, Demirbas E, Ergin A. The effects of cyclopentolate on ontraocular pressure and retrobulbar hemodynamics in patients with pseudoexfoliation syndrome and pseudoexfoliation glaucoma. *Eur J Ophthalmol* 2004; **14**: 394–400.
- 3 Loukovaara S, Immonen I, Koistinen R, Hillesmaa V, Kaaja R. Inflammatory markers and retinopathy in pregnancies complicated with Type I diabetes. *Eye* 2005; **19**: 422–430.
- 4 Linnik Yu V. Latest investigations on Behrens–Fisher problem. *Sankhya A* 1966; **28**: 15–24.
- 5 Kendall MG, Stuart A. *The Advanced Theory of Statistics*, Vol. 2. Charles Griffin and Co.: London, 1973, p 484.
- 6 Lehmann EL. *Testing Statistical Hypotheses*. John Wiley and Sons Inc.: New York, 1959, p 187.
- 7 Tsakok AD. A solution to the generalized Behrens-Fisher problem. *Metron* 1978; **36**: 79.
- 8 Tsakok AD. A generalization of the Borel–Cantelli lemma. *Metron* 1995; **53**: 25.
- 9 Tsakok AD. Comment on visual acuity. *Ophthal Epidemiol* 2002; **9**: 347.
- 10 Tsakok AD. A test of fit satisfying some optimality criteria non-asymptotically. *Metron* 1978; 36: 105.
- 11 Tsakok AD. *Statistics and the Unified Field*. AD Tsakok Mathematical Centre: London, 1987.
- AD Tsakok

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Sir, Reply to Dr AD Tsakok

We highly appreciate Dr AD Tsakok's interest in our recently published paper.¹ In his letter,² he suggests a different approach to the statistical problem which we solved using either Student's two-sample *t*-test or analysis of variance (ANOVA). Dr Tsakok argues that the shortcoming of our statistical approach lies in the assumption of equal variances between groups (Behrens-Fisher problem^{3,4}). In his opinion, this assumption renders the applied tests unsuitable for the purposes to which they were put. Dr Tsakok advocates a statistical test that he himself has developed to compare quantitative data between multiple groups,⁵ and which is already available as commercial software.

¹ Halberstadt M, Chatterjee-Sanz N, Brandenberg L, Koerner-Stiefbold U, Koerner F, Garweg JG. Primary retinal