Visual field progression: comparison of Humphrey Statpac2 and pointwise linear regression analysis

Abstract • Background: Humphrey Statpac2 ‘glaucoma change probability analysis’ is a widely available analysis technique to aid the clinician in the diagnosis of glaucomatous visual field deterioration. A comparison of this technique with the more recently described pointwise linear regression analysis (PROGRESSOR) is given.

• Methods: Series of visual field data from a group of nine eyes of nine patients with normal-tension glaucoma were selected. Each series had 16 fields with mean follow-up of 5.7 years (SD 0.6 years). Statpac2 ‘glaucoma change probability analysis’ was used to define test locations that had unequivocally deteriorated in the last three fields of each series. The accuracy of both Statpac2 and PROGRESSOR in providing early detection of these deteriorated locations was assessed.

• Results: The sensitivity and specificity of the two techniques in predicting deteriorated locations were similar when a rate of luminance sensitivity loss of faster than 1 dB/year (2 dB/year for outer locations beyond 15 deg of eccentricity) with a slope significance of P<0.10 was used as the regression definition of deterioration. The difficulties of comparing two techniques in the early diagnosis of field progression without a true external standard for field loss are illustrated.

• Conclusions: PROGRESSOR closely emulates the performance of Statpac2 in detecting sensitivity deterioration at individual test locations. This new technique, which uses all available data in a field series and gives the rate of sensitivity loss at each location, may provide a clinically useful method for detecting field progression in glaucoma.

Introduction

Modern automated perimeters yield sensitive and objective assessment of the central visual field. However, the detailed numerical output from an automated perimeter may be less amenable to the traditional inspection and intuitive analysis for field deterioration performed by the clinician. Inter-test fluctuation in measuring the threshold also makes intuitive analysis of any deterioration difficult, and even experienced observers show poor agreement on what constitutes field progression [19]. A diagnosis of unequivocal visual field deterioration using intuitive analysis may require many field tests performed over several years.

Statistical analysis techniques which aid clinicians in the interpretation of serial automated perimetry data have been described. Some techniques evaluate the trend of summary measures of sensitivity of the field as a whole or in part against time of follow-up [8, 16, 21]. Regression analysis of the average, age-corrected sensitivity of the field (mean deviation or defect, MD) has proved useful in the follow-up of glaucoma [18]. Other methods perform pointwise analysis, in which each test location is analysed separately [15, 20]. Linear regression analysis of Humphrey MD allows straightforward
interpretation of overall change but may underestimate clinically important focal deterioration [20]. Pointwise analysis methods have been described which, by preserving diagnostic spatial information may allow early detection of localised field deterioration. A widely available pointwise analysis technique is the ‘glaucoma change probability analysis’ which constitutes part of the Humphrey Statpac2 software package [6]. This program allows selection of two early visual fields as a ‘baseline’. Subsequent visual field tests are directly compared to this baseline. Significant change from baseline in the measured threshold at any location is determined by comparison with a reference database of visual fields from stable glaucoma subjects. This change is displayed as symbols indicating deterioration, improvement or stability. This ‘glaucoma change probability analysis’ has been shown to correlate well with routine clinical evaluation of progression of visual field changes [17]. Close agreement has also been found between the ‘glaucoma change probability analysis’ and a traditional intuitive criterion, fixed at 5 dB loss, for identifying visual deterioration at individual points [13].

Intrinsic to the method underpinning Statpac2 ‘glaucoma change probability analysis’ is the detection of change in sensitivity purely from two baseline fields. It represents an event type analysis [7]. Previously we have described an alternative method for evaluating progression, based on linear regression analysis of pointwise sensitivity values against time of follow-up, which importantly uses all the subject’s field series [14]. This method, in contrast to Statpac2 ‘glaucoma change probability analysis’, represents a trend type analysis. A computer software package, described fully elsewhere [4], has been developed which uses this method of pointwise linear regression to identify field locations that demonstrate statistically significant rate of sensitivity loss. The results are given in a single colour-coded display to allow the clinician to clearly appreciate the rate of loss at individual test locations.

Previously we have shown, by curve-fitting experiments on deteriorating locations from untreated glaucomatous eyes with long historical field series, that the pointwise linear regression model adequately describes pointwise glaucomatous sensitivity decay in a group of untreated normal tension glaucoma patients [11]. Complex mathematical models were found to closely fit pointwise sensitivity against time of follow-up but at the expense of modelling the high level of variability inherent in some series of field data, thus generating poor predictions of field change. The statistical nature of the linear model allows good predictions without this confounding effect.

In this paper we directly compare Statpac2 ‘glaucoma change probability analysis’ with pointwise linear regression analysis. We assess the ability of the two methods to correctly predict the sites of test locations that subsequently deteriorate in sensitivity within the visual field. The main purpose of this study is therefore to evaluate whether pointwise linear regression analysis can emulate the predictive performance of Statpac2 ‘glaucoma change probability analysis’ in identifying change in progressive glaucoma.

Materials and methods

Subjects

Subjects were selected from a total database of 220 normal-tension glaucoma (NTG) patients followed at Moorfields Eye Hospital. NTG was defined as intraocular pressure (IOP) <21 mm Hg, confirmed following 24 h IOP phasing, and optic disc appearance and initial visual field loss consistent with a clinical diagnosis of glaucoma. The patients were untreated during the length of follow-up. Patients were not selected randomly. The Humphrey Statpac overview printouts of all the patients who had undergone at least 17 visual field tests and who had acceptable reliability indices (less than 20% false positive responses and fixation losses) were examined by an experienced clinician. One eye was selected from each of nine patients in whom the overview printout showed initial visual field loss and exhibited field deterioration on clinical judgement. Each eye had a series of 16 fields. Inspection of the patients’ clinical notes excluded, as far as is possible, the development of cataract as the cause of the decline in visual function. Neither Statpac2 ‘glaucoma change probability analysis’ nor pointwise regression analysis were used at the selection stage, since this might have allowed biased selection of patients showing a precipitant, or a broadly linear pattern of deterioration, respectively. Deteriorating eyes were selected to guarantee sufficient individual progressing locations to allow meaningful comparison of the methods.

Selected subjects had similar follow-up periods (mean 5.6 years, SD 0.6 years; range 3.2-6.4 years) and similar intervals between each field (mean 0.35 years, SD 0.09; range 0.17-0.62 years). As a global summary the first field for each selected eye had a mean Humphrey MD of -6.4 dB (range -11.7 to -4.4 dB) and mean corrected pattern standard deviation (CPSTD) of 6.8 dB (range 3.0-13.3 dB). These summary measures worsened for the whole sample to a mean MD of -11.5 dB (range -17.9 to -8.7 dB) and a mean CPSTD of 10.4 dB (range 7.6-16.0 dB) at the 16th field. Statpac2 provides linear regression of each subject’s MD against time of follow-up. In all the selected eyes the rate of MD deterioration was significant at least to P<0.01 when com-

Fig. 1 Humphrey Statpac2 ‘glaucoma change probability analysis’ for one of the subjects. The series of 16 fields shows a gradual increase in the size and depth of the inferior arcuate visual field defect. The series covers a follow-up period in excess of 7 years. The two baseline visual fields are shown in the top left corner close to the graph showing regression analysis of the mean defect against time (significant decline at P<0.01 in this example). The subsequent fields in the series have been compared to the baseline, and any pointwise change is displayed by a symbol indicating significant deterioration (filled triangle), significant improvement (open triangle) or stability (dot). The final three fields of the series (indicated by arrows) were used to determine the definition of deterioration. As an illustration of how the definition for deterioration was defined, the ringed locations in the inferonasal field of the final three fields indicate that these locations satisfy the criteria for ‘definite deterioration’, i.e. a filled triangle at the same location at least two of the final three fields.