Abstract
The unique facial appearance associated with fetal alcohol syndrome (FAS) is emphasised in diagnosis, which relies, in part, on the comparison of linear measurements of facial features to population norms. We explore the use of shape analysis as an alternative diagnostic tool for FAS. This paper implements General Procrustes Analysis to compare the FAS facial shape with the normal facial shape. No statistically significant difference was found between the FAS and normal facial shapes.

1. Introduction
Fetal Alcohol Syndrome (FAS) is a clinical condition caused by excessive maternal consumption of alcohol during pregnancy. FAS has come to be accepted as the leading identifiable preventable cause of mental retardation and neurological deficit in the Western world [1] although data from poorer areas of the world with much higher prevalence is not readily available. Diagnosis of FAS depends on evidence of growth retardation, CNS neurodevelopment abnormalities and a characteristic pattern of facial anomalies, specifically a short palpebral fissure length, smooth philtrum, flat upper lip and flat midface [2].

A confident diagnosis of FAS, based on linear facial measurements, can at present only be made by an expert dysmorphologist [3]. Statistical analysis on data for FAS diagnosis thus far has suffered from a lack of quantitative scaling. There is however a lot of research into providing a quantitative case definition for the disorder based on the facial anomalies characteristic of FAS. Objective quantitative scales not only improve accuracy and precision, but also establish a common numeric language for communicating outcomes in medical records and in the medical literature [4].

Quantitative descriptions of the FAS phenotype to date have been based on linear measurements. In this paper, we explore the use of shape analysis to distinguish between subjects with FAS and normal subjects. Shape is defined as all the geometrical information that remains when location, scale and rotational effects are filtered out from an object [5]. Two shapes can be compared by adjusting for size and superimposing one shape on the other. The differences that remain are then due to shape dissimilarity. Landmarks are points of correspondence on each shape object that match between and within populations. Shape analysis methods play a valuable role after identification of facial landmarks that are considered important in the diagnosis of FAS. Facial shapes may be compared and averaged in terms of the relative positions of a set of landmarks[3, 6]. In their report on the facial effects of fetal alcohol Clarren et al. [3] utilized triangles defined by sets of three landmarks for analysing facial landmarks. The mean shapes of these triangles were compared between subjects more-exposed or less exposed prenatally to alcohol. Pattern profile analysis is a simple method of classifying, portraying and comparing patterned deviations from the norm[7]. Moore et al. [8] used this method to quantify the elements of the FAS facial phenotype and to extend the quantitative phenotype to individuals who exhibited less severe or incomplete manifestations of prenatal alcohol exposure. Their results corroborated previous observations that individuals diagnosed with FAS exhibit, on average, small heads (microcephaly), small faces, short palpebral fissures, and hypoplastic midface.

This paper reports on a comparison of the clinically relevant facial landmarks of FAS subjects with Normal subjects using Generalised Procrustes Analysis (GPA).

2. Shape Analysis
2.1 Feature Extraction
The study population consisted of images obtained during the screening of first-grade children from disadvantaged communities in the Gauteng and Northern Cape Provinces of South Africa for FAS. The subjects were appraised by three independent dysmorphologists and images of subjects with a clinical diagnosis of FAS and “Normal” children were used in this study. Images of 56 normal and 24 FAS subjects were available from the data base.

The images were acquired through stereo-photogrammetry. These images were used to obtain 3D coordinates of facial landmarks [9]. The acquisition tool consists of control frame with a pair of high resolution digital cameras. The cameras used to obtain the images are simultaneously triggered by use of remote control. The tool was designed with eleven well distributed retro-reflective control markers whose three-dimensional co-
ordinates are known and these are exploited in the calibration of the images.

Facial landmarks cited in literature as phenotypical of the FAS facial profile were considered in the analysis. These also have the advantage that they occur on extremes of curves and contours making measurements easier. Included were the right and left endocanthion (medial corners of the eyes), right and left exocanthion (lateral corners of the eyes), subnasale (lowest point on the tip of the nose), stomion (highest point on mouth directly below the subnasale), right and left cheilion (corners of the mouth), the midpoint of the philtrum furrow between the subnasale and the stomion and the two philtrum ridges on either side of the stomion on the upper vermillion boarder. These points are shown in Figure 1 below.

Together with the coordinates of the philtrum ridges at the upper vermillion line, both cheilion and the stomion were used to explore lip thinness. The inner and outer canthion on the eyes were used to explore palpebral fissure length. The midpoint of the philtrum furrow, the subnasale and the philtrum ridges were used to explore philtrum smoothness.

The GPA algorithm presented below was used to align the configurations.

![Figure 2: The plot of feature coordinates to form a configuration.](image)

### 2.2 Generalised Procrustes Analysis

The Procrustes method for comparing shapes is any of a number of methods based on fitting all \( n \) landmark points for \( N \) shapes using various fitting procedures for optimal superimposing of landmarks. Shape can be described by locating a finite number of points on the shape outline or by locating landmarks. An \( n \)-point/landmark shape in \( k \) dimensions can be mathematically represented by concatenating each dimension into a \( k \times n \)-vector. By establishing a coordinate reference with respect to position, scale and rotation true shape representation can thus be obtained. The coordinate reference or pose aligns all the shape objects in question. Optimum superposition of shape objects is achieved when translation and rotation effects are adjusted so as to minimize the distances between landmarks [10]. Various minimization criteria exist but the most popular is that which minimizes the sum of the squared distances between corresponding points [10]. Generalised Procrustes superimposition uses such criteria by taking \( n \) shapes and resizing them to their centroid size and then aligning them to minimize this sum.

The GPA algorithm is:

1. Choose an initial estimate of the mean shape or configuration. The initial shape in the set will do.
2. Align all the remaining shapes to the mean shape using the Procrustes superposition.
3. Re-calculate the estimate to the mean from the aligned shapes.
4. If the estimate mean has changed return to step 2.

Convergence is declared when the mean shape does not change significantly within an iteration [11]. The Procrustes mean shape is found by the equation:

\[ \text{Mean Shape} = \frac{1}{n} \sum_{i=1}^{n} \mathbf{X}_i \]
\[ \bar{x} = \frac{1}{N} \sum_{i=1}^{N} x_i \]

Where \( N \) = the number of shapes

The Procrustes mean shape and Procrustes fit coordinates are used to plot aligned shape configurations as shown in figure 3.

Figure 3: Unregistered configurations on the left and registered configurations on the right; Normal subjects (top) and FAS subjects (bottom).

2.3 Statistical Analysis of difference in means

The Procrustes mean configurations for each group were plotted using the coordinates calculated above and the two were compared for difference in means. Goodall's F test was used to examine differences in mean shape between the two groups (Table 1). The large p-value indicates that there is no statistically significant difference in the mean shapes of the two groups. The shapes of the two groups are superimposed in Figure 4.

<table>
<thead>
<tr>
<th>Description</th>
<th>Value</th>
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<tr>
<td>Between Group Distance</td>
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<tr>
<td>F-Score</td>
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<tr>
<td>p</td>
<td>0.956102</td>
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<td>Within Group Variance Normal Subjects</td>
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<tr>
<td>Within Group Variance FAS Subjects</td>
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Table 1: Results of Goodall’s F- test
3. Discussion

This study confirms that the effects of prenatal alcohol exposure on the face fall along a continuum instead of occurring as discrete traits. The mean shape difference between FAS and Normal subjects in this sample is very small as can be observed from figure 4 above. Goodall’s test for difference in means confirms that for the study sample the facial shape range of FAS subjects’ overlaps with the facial shape variability of normal subjects. The within group variability of the two groups is almost identical and together with the insignificant p-value (0.956102) might suggest that there is no objective line of division between the FAS and Normal groups.

Figure 5 illustrates this overlap of features. The top image is a FAS subject and the bottom image a normal subject. Both subjects have smooth long philtrums and their upper lips have similar shapes. In the sample this occurrence is not unique. GPA attempts to compare shapes after removing scaling, rotation and position. In an ideal sample it would be possible to delineate the typical FAS facial phenotype of smooth philtrum, small palpebral fissure length and thin upper lip from that of normal subjects based on comparison of mean shape alone.

Microcephaly is of importance in the craniofacial appearance of FAS subjects. Moore et al [8] suggest that the commonly used clinical descriptors of long philtrum and wide spaced eyes often employed in the diagnosis of children with FAS must be seen in relative terms. That is, the long philtrum and short palpebral length are not measurably different from normal but appear so in relation to the overall reduction in cranial size.

It needs to be noted however that the sample size might be too small to make a conclusive assessment of shape difference and it is recommended that the study be repeated with a larger sample size. Another recommendation is implementation of more advanced feature extraction methods to annotate the facial features. By including more points on the outline of the features as shown in Figure 6 a more accurate representation of the
features can be obtained and information lost in making rudimentary estimations of the features can be used in shape analysis.

References: