Institution: University of Dundee		
Unit of Assessment: UoA10 Mathematical Sciences		
Title of case study: Software development for measuring dental clinical outcomes		
Period when the underpinning research was undertaken: 2013 - now		
Details of staff conducting the underpinning research from the submitting unit:		
Name(s):	**Role(s) (e.g. job title):**	**Period(s) employed by submitting HEI:**
Ping Lin	Professor of Numerical Analysis	2007 - present
Period when the claimed impact occurred: 2015 - present		
Is this case study continued from a case study submitted in 2014? N		

1. Summary of the impact

Clefts of lip and palate affect around 1 in 700 live births, leading to lifelong problems. The best age at which to attempt surgical repair remains unclear due to variation in treatment practices and difficulty in obtaining accurate and objective measures to differentiate outcomes. Lin and co-workers at Dundee have addressed this challenge by developing the first fully automatic and objective landmarking diagnostic scoring tool. The tool utilises digital images, numerical analysis techniques (computational geometry and image segmentation) and an index algorithm. These are combined in an automated, user-friendly software package that facilitates rapid capture and accurate scoring. The measurement tool has been adopted as the method of choice in a multi-million dollar global trial to identify optimal timing for surgical intervention. It has transformed precision and objectivity of the scoring, eliminated human error and delivered significant gains in efficiency.

2. Underpinning research

The underpinning research is interdisciplinary, resulting from a joint project with Professor Peter **Mossey** (Dundee, UoA 3). Research at Dundee led to an enhanced digital method based on oral scanning that replaces the need for traditional plaster moulds in clinical investigations of patients with clefts of lip and palate. The utility of this digital process relies on a novel method of measurement - the Modified Huddart Bodenham (MHB) index occlusal scoring system developed by **Mossey** and co-workers **[R1]**. This scoring system can be manually implemented, but this renders it time-consuming and relies on the subjective interpretation of images by highly trained clinicians. Research by **Lin** and co-workers was key to the development of the first fully Automatic Landmarks Recognition (ALR) diagnostic scoring tool. The ALR tool facilitated a step-change in the efficiency, objectivity and accuracy of the digital scoring process. The tool automatically applies the MHB index to digitally scanned images using numerical analysis techniques (surface and data fitting, computational geometry and image segmentation) to form a user-friendly software package that facilitates rapid, objective and accurate diagnoses. The software was first developed using the 3D CAD Rhinoceros C++ software development kit and then latterly directly using Python.

Major research milestones associated with the development of the tool are:

Reduction of superfluous control points. Data sets derived from scanned piecewise triangular mesh rendering of images of teeth (called a 3D digital model) are both large in size and ill-suited to accurate shape characterisation. Such data are commonly fitted by non-uniform rational B-splines (NURBS). **Lin** and co-workers' recent developments in spline interpolation **[R2,R3]** corrects NURBS deficiencies whilst preserving their advantages. **Lin's** work significantly

reduces the number of control points, avoids gaps and overlaps at interactions of surfaces and permits local refinement and coarsening.

Novel algorithms for (3D) image segmentation and Automatic Landmarks Recognition (ALR). Locating an individual tooth or a pair of teeth and identifying landmarks from upper and lower arches for assessment in the 3D digital model is extremely challenging. The specifics of the MHB index requirements and the complex geometry and topology of human teeth presented unresolved challenges. To overcome these difficulties, image segmentation methods **[R4,R5]** and a full ALR process **[R4,R6]** were developed from scratch by **Lin** and co-workers and shown to be highly effective **[R4,R6]**. The utility and accuracy of the ALR tool are obtained by:

(i) using principal component analysis, fine-tuning the vertical axis to accurately identify the position and orientation of the 3D digital model **[R4,R6]**.

(ii) using local maxima (peaks) in the vertical direction to automatically provide an initial selection of the landmarks (the tips or cusps of teeth) **[R4,R6]**.

(iii) identifying the shape and boundaries of each tooth, extracting/computing surface gradient and edge curvature information and flood-filling from each peak obtained in (ii) until reaching a relatively large negative curvature (a feature of the join or crease between tooth and gum) **[R4,R5]**.

(iv) removing unwanted peaks on gums and the roof of the mouth obtained in (ii) through a careful justification using the criteria in (iii) **[R4]**.

(v) approximating the jawline through data fitting of identified tooth landmarks to formulate a tooth assignment problem **[R4]** and using a combination of machine learning on tooth characteristics (such as total surface area) and linear programming methods **[R4,R6]** to recognise and label each tooth (as an incisor, canine, premolar or molar) and its landmarks.

Automatic occlusal scoring computation and annotation. Based on the MHB index **[R1]**, geometric information from landmarks identified on the generalised spline surface is used to generate a cumulative score from all the identified tooth pair scores. **Lin** and co-workers improved the accuracy of scoring by measuring the distance between the two fitting spline surfaces of opposing teeth. The discrepancy between two surfaces was measured using the symmetric Hausdorff distance **[R2,R3]**.

3. References to the research

[R1] Mossey, PA, Clark, JD & Gray, D (2003), Preliminary investigation of a modified Huddart/Bodenham scoring system for assessment of maxillary arch constriction in unilateral cleft lip and palate subjects, *European Journal of Orthodontics*, vol. 25, no. 3, pp. 251-257.DOI: 10.1093/ejo/25.3.251

[R2] Ma, X, Martin, C, McIntyre, G, Lin, P & Mossey, P (2017), Digital three-dimensional automation of the modified Huddart and Bodenham scoring system for patients with cleft lip and palate, *Cleft Palate-Craniofacial Journal*, vol. 54, no. 4, pp. 481-486. DOI: 10.1597/15-340

[R3] Martin, C, Ma, X, McIntyre, G, Wang, W, Lin, P, Chalmers, E & Mossey, P (2016), The validity and reliability of an automated method of scoring dental arch relationships in unilateral cleft lip and palate using the modified Huddart-Bodenham scoring system, *European Journal of Orthodontics*, vol. 38, no. 4, pp. 353-358. DOI: 10.1093/ejo/cjw031

[R4] Woodsend, B, Koufoudaki, E, Mossey, PA & Lin, P (2020), Automatic Recognition of Landmarks on Digital Dental Models, *arXiv*. <https://arxiv.org/abs/2012.12946>

[R5] Wang, Y, Ji, G, Lin, P & Trucco, E (2013), Retinal vessel segmentation using multiwavelet kernels and multiscale hierarchical decomposition, *Pattern Recognition*, vol. 46, no. 8, pp. 2117-2133.DOI: 10.1016/j.patcog.2012.12.014

[R6] Woodsend, B, Koufoudaki, E, Lin, P, McIntyre, G, El-Angbawi, A, Aziz, A, Shaw, W, Semb, G, Reesu, GV & Mossey, PA (2020), Development of intra-oral automated landmark recognition (ALR) for dental and occlusal outcome measurements, *BioRxiv*.
DOI: 10.1101/2020.12.16.423094

4. Details of the impact

Clefts of lip and palate affect around 1 in 700 live births, leading to lifelong problems with eating and speech often combined with debilitating psychological impact. Poor regional comparability regarding the incidence, treatment and outcome of cleft births is confirmed in the *Eurocleft* project, which highlights the vast number of different practices and protocols being used to treat even one cleft subtype. This variation is attributable largely to differences in measurement and classifications. As such, the optimal timing for surgical intervention remains a contentious issue with arguments and counter arguments presented for intervention at six and 12 months, respectively **[E2]**. Precise and time-efficient measurement is critical in the acquisition and interpretation of data that helps develop knowledge of cleft birth defects, identifies optimal treatment practices and enables cross comparisons for cleft outcomes. The development by Lin and colleagues of the first fully automatic diagnostic (ALR) tool provided the precision, efficiency and objectivity required to meet these measurement demands:

> *"It is important to highlight the importance of this innovation in standardizing the measurement process and eliminates humans' errors. This is a long-waited innovation of automatic landmark recognition improves precision, offers economic benefits, and facilitates the analysis of global data. The developed technology provides a clear example of transferring the sophisticated technology of image analysis and artificial intelligence to clinical applications."* **[E1]**

The automatic landmarks recognition diagnostic tool (ALR tool) was first applied to 3D digital models in 2016 **[R3]** and subsequently in 2019 **[R4,R6]**. Data were gathered from 53 patients with cleft lip and palate from the *Cleft Care Scotland* database and the results obtained by the automatic tool were compared with scores given by three experts in orthodontics and craniofacial abnormalities. The comparative process demonstrated significant advantages of the ALR in terms of speed and objectivity of scoring: experts took over three minutes to assess one case, in contrast with 40 seconds for the ALR tool. Additionally, it was shown through statistical methods that the ALR tool was also more accurate than the existing, manual method of MHB scoring by highly skilled clinicians:

> *"No research team until now has undertaken full automation of the* [scoring] *system… To do this* [scoring] *visually is not only time-consuming at around three minutes per case, but the issues with accuracy… risk inappropriate conclusions being drawn for the individual patient and where comparisons are being made with reference data in research. The automated system calculates the result instantaneously."* **[E4]**

The consultants involved highlight the novelty of the automatic tool, the efficiency gains it produces, and the importance placed on the enhanced accuracy and objectivity that it delivers **[E3]**. The importance of the accuracy of the tool is further highlighted in relation to surgical interventions and outcomes, where incorrect or inaccurate scoring can lead to subsequently poor surgical outcomes **[E4]**.

A multi-million dollar global Randomised Controlled Trial (RCT) funded by the US National Institute of Health and based at the University of Manchester entitled *Timing for Primary Surgery for Cleft Palate (TOPS)* was set up to resolve questions regarding patient outcomes following surgical intervention at six and 12 months. The need for extremely sensitive measurements to

differentiate the data recording occlusal outcomes (tracing assessments of key features in patients' mouths at 1, 3 and 5 years of age), and the proven success of the ALR tool in the Cleft Care Scotland test, led the TOPS trial team to adopt the automated tool as the method of choice for the global RCT.

The significance of the decision is noted by one expert (not directly engaged with either the Cleft Care Scotland or TOPS trials):

> *"The development* [of the ALR tool] *provides an unprecedented opportunity to conduct a highly reproducible and accurate scoring process. The utilisation of this innovative software for the TOPS trial is a global recognition and acknowledgement of the achievement*." **[E1]**

In 2019 the Dundee team used the software to score patient data from the trial: 558 patients from 23 hospitals and health centres: 10 in the UK, 12 in Scandinavia (six in Sweden, two in Denmark and two in Norway) and one in Brazil. It proved highly successful in terms of efficiency, precision and objectivity of the scoring process. Evidence of the efficiency gain provided by the ARL tool is highlighted by one of the clinicians involved with the TOPS trial who notes that over 60 hours of work would typically be required to score the data using trained staff. In comparison, the ARL tool took just five hours.

> "*this* [scoring] *would previously have taken each researcher 27.9 hours… Moreover, due to the errors involved in human assessment, this is normally repeated by a second observer, with 20% being reassessed... In total, this would take 67 hours, but will be undertaken instantaneously using the innovative automated system*." **[E4]**

With another consultant involved in the TOPS trial commenting on the benefits of the tool, noting that it "*has transformed precision / objectivity of the scoring, has unburdened researchers and eliminated human error*." **[E2]**

In summary, the development of the fully automatic diagnostic tool has played a central role in the determining a successful and usable outcome from the TOPS global RCT. The speed, accuracy and objectivity of the tool proven in the Cleft Care Scotland trial caused the TOPS trial group to rethink their approach to scoring. The ALR diagnostic tool has proven to be uniquely capable of delivering the accuracy and efficiency required to differentiate output measures related to the timing of surgical intervention.

In the words of one Specialist in Orthodontics, "*this will ultimately raise the quality of cleft care globally*" **[E3]**. The utility of the automatic tool and its potential to deliver a significantly improved patient experience in a global context is further highlighted by an Orthodontic Consultant who states:

> "*The impact of this development is enormous and is a 'game-changer' in the field"* **[E4]**

5. Sources to corroborate the impact

Letters of support:

[E1] Honorary Consultant in Maxillofacial Surgery, University of Glasgow.

[E2] Clinical Senior Lecturer and Consultant in Orthodontics, TOPS dento-facial outcome lead, University of Manchester (Clinician on Manchester trial)

[E3] Specialist in Orthodontics, Falmouth Health Centre (Clinician on Cleft Care Scotland trial)

[E4] Tayside Orthodontic Consultant, Dundee Dental Hospital, Perth Royal Infirmary and Ninewells Hospital (Clinician on Cleft Care Scotland and Manchester trials)