Institution: University of Manchester

Unit of Assessment: 11 (Computer Science and Informatics)

Title of case study: Improving healthcare and animal welfare using statistical shape models

Period when the underpinning research was undertaken: 2000 – present

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:
Timothy F. Cootes	Professor	1991 – present
Chris Taylor	Professor	1970 – present
Carole Twining	Lecturer (2010 – 2020) RCUK Fellow (2005 – 2010) PDRA (1999 – 2005)	1999 – 2020
Claudia Lindner	Research Fellow (2016 – present), PDRA (2014 – 2016)	2014 – present
Rhodri Davies	PDRA (2002 – 2004)	2002 – 2004

Period when the claimed impact occurred: 1 August 2013 – 31 December 2020

Is this case study continued from a case study submitted in 2014? N

1. Summary of the impact

Reliable automatic methods for locating bones and organs in medical images are critical for many clinical and commercial challenges. Researchers at The University of Manchester have developed novel statistical shape and appearance models, which are capable of locating the outlines of structures in medical image, to a more robust and accurate level than was previously possible.

Four companies are using this technology to deliver fundamental improvements in their operations. This is benefiting adult and paediatric patients worldwide, saving clinicians vital time, and improving animal welfare in food production. Specifically this research has:

- Produced IP valued at [text removed for publication]
- Benefitted 50,000 joint replacement patients globally
- Diagnosed over 100,000 child growth abnormalities across the EU
- Enabled a global poultry company to improve accuracy and throughput of bird health.

2. Underpinning research

Research, led by Taylor and Cootes, at The University of Manchester (UoM), built on their previous work that demonstrated how interpretation of a particular class of images could be based on generative models of shape and appearance, learnt from a training set of similar images. During the period 2000-2016, they extended the approach, wrote the definitive paper on the topic [1], developed new techniques for automatically constructing statistical models of structures either from sets of surfaces (extracted from images) or from raw images themselves, and developed a more robust method of locating the outlines of structures in images using such models.

This research:

i) demonstrated how statistical models of shape and appearance could be constructed (from annotated images) and fitted automatically to previously unseen images of the same class [1].

ii) showed how shape models of 3D structures (bones, organs) could be constructed from just the surfaces extracted from example images [2].

iii) demonstrated how models of shape and appearance could be built automatically from unlabelled training images [3], making it practical to create new models quickly and accurately from 3D image data.

iv) developed a method for locating the points of the model using machine learning techniques to vote for their position (the Random Forest Regression Voting Constrained Local Model (RFRV-CLM) [4]). This method enables accurate fitting even on uncommon shapes. This is essential for use on clinical images, where disease diagnosis is the aim and so unusual (i.e. pathological) shapes are of most interest. This technique was shown to be more accurate than any previous approach and still represents the state-of-the-art for many clinical imaging problems.

Since 2012, research at UoM has applied the RFRV-CLM to identify and measure the shapes of bones in various types of clinical images, including knees, hips, vertebrae [4] and skulls [5]. This research enabled models to be built and evaluated for each anatomical structure, demonstrating that the models can locate bones accurately and reliably enough to be useful for clinical applications.

3. References to the research

This research has received over GBP1,900,000 of funding from EPSRC, MRC, Wellcome/NIH and NIHR. It has been published in top journals in the field [1,3,5], and presented at internationally leading conferences; [2] winning best paper prize, and [4] being presented at the European Conference on Computer Vision, one of the top two conferences in the field. Citations are from google scholar, in November 2020.

[1] T.F.Cootes, G.J. Edwards and C.J.Taylor. (2001) Active Appearance Models, *IEEE Pattern Analysis and Machine Intelligence* (PAMI), 23 (6), pp.681-685, DOI:10.1109/34.927467 (**5909 citations**, *24/5718 in PAMI all-time citation list*)

[2] R.H.Davies, C.J.Twining, T.F.Cootes, J.C.Waterton,C.J.Taylor, 2002, 3D Statistical Shape Models Using Direct Optimisation of Description Length, Proc. European Conference on Computer Vision 2002, Vol.3, pp.3-20 DOI: 10.1007/3-540-47977-5_1 (**275 citations**)

[3] T.F. Cootes, C.J.Twining, V.S.Petrovic, K.O. Babalola and C.J.Taylor (2010), Computing Accurate Correspondences across Groups of Images, *IEEE Trans. PAMI* Vol. 32 (11) pp.1994-2005, DOI:10.1109/TPAMI.2009.193 (**91 citations**)

[4] T.F. Cootes, M. Ionita, C. Lindner, and P. Sauer. (2012) Robust and Accurate Shape Model Fitting using Random Forest Regression Voting. Proceedings of the 12th European Conference on Computer Vision (ECCV 2012, Part VII), Florenze, Italy. Springer-Verlag *Lecture Notes in Computer Science* 7578, pages 278-291, DOI:10.1007/978-3-642-33786-4_21 (**287 citations**)

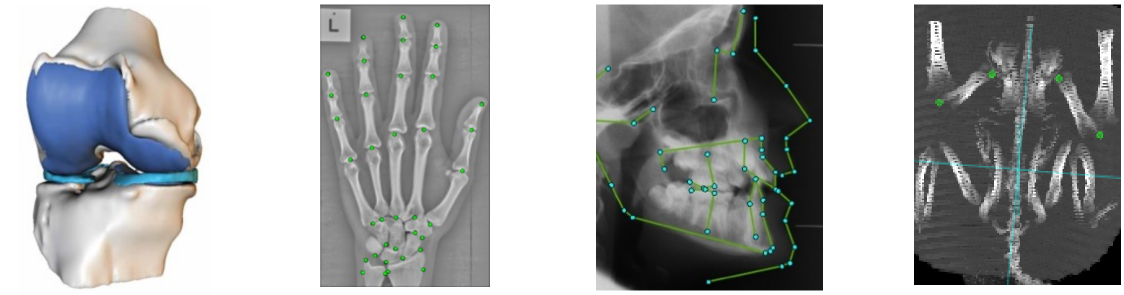
[5] C.W. Wang, C.T. Huang, J.H. Lee, C.H. Li, S.W. Chang, M.J. Siao, T.M. Lai, B. Ibragimov, T. Vrtovec, O. Ronneberger, P. Fischer, T.F. Cootes and C, Lindner. (2016) A benchmark for comparison of dental radiography analysis algorithms. *Medical Image Analysis*, Vol. 31, pages 63-76, DOI: 10.1016/j.media.2016.02.004 (**98 citations**)

This paper describes the Cephalometric BoneFinder® module which won the first prize in the 2015 IEEE International Symposium on Biomedical Imaging (ISBI) Grand Challenge for dental X-ray image analysis.

4. Details of the impact

Context

The underpinning research [1-6] has established a fundamentally new generic approach to image interpretation. This has been applied across multiple industries (Figure 1), replacing expensive to develop and maintain 'hand-crafted' solutions to specific problems and automating essential, yet time consuming tasks. Broadly, this has provided two main benefits: (i) improving patient outcomes through improved treatment and diagnosis; and (ii) improving animal welfare.



Surgery planning | Bone age estimation | Orthodontics | Disease in chickens

Figure 1. Visual application of the research across different industries, including surgical planning, paediatrics, orthodontics and animal disease

(i) Improving patient outcomes through improved treatment and diagnosis processes

a) Improved planning for implant surgery

In 2001, Imorphics Ltd was formed as a spin-out from the UoM, to apply the 3D statistical modelling and image analysis techniques (including [1-3]) to medical image analysis problems. This analysis is used in the planning of knee and hip replacement surgery. This requires careful measurements to be taken of the existing bones from images, which is time consuming, and undertaking this manually is estimated to take up to an hour of a clinician's time, per replacement.

[Text removed for publication].

b) Increased efficiency in diagnosis of paediatric growth abnormalities

Across Europe, 3-5% of children are tested annually for possible growth disorders. This testing is done through assessing their apparent skeletal age from a hand X-ray, and comparing to their actual (chronological) age – a significant difference in the two is a sign of a bone-growth disorder. Traditionally, manually undertaking this assessment is both time consuming and imprecise.

In 2008, Visiana, a Danish company, used the UoM model based image analysis techniques [1] to automatically locate outlines of bones in radiographs of children's hands. The "Active Appearance Model" (AAM) algorithm [1] underpins their main product, BoneXpert [C], a system for estimating the apparent skeletal maturity of a child. Whilst previous research has attempted to automate this process, Visiana have confirmed that the AAMs from UoM "*were the first solution to accurately and reliably locate the bones*" [C].

Visiana confirm the UoM models "*are at the core of [their] BoneXpert medical device*" [C]. BoneXpert is both more accurate than human experts (errors of about 0.4 years compared to about 0.8 years for radiologists) and faster (a few seconds rather than 2-20 minutes). As of July 2020, BoneXpert had been adopted by 150 major childrens' hospitals, mainly in Europe (increasing by around 1 per month), collectively conducting approximately 100,000 diagnoses per annum [C], at EUR9 or 12 each. In the period 2014-2020, Visiana have performed over 400,000 diagnoses with BoneXpert, leading to a cumulative turnover of over EUR2,000,000 (GBP1,700,000) with current turnover of EUR700,000 (GBP600,000) *per annum* [C].

The Visiana CEO has confirmed, "*Before getting BoneXpert, 88% of responding clinics reported image assessment taking more than 2 minutes. After getting BoneXpert that* *reduced to only 19%, suggesting a considerable saving of clinician's time. It has been found to be so accurate and reliable, that 30% of radiologists have completely replaced manual readings with BoneXpert*" [C].

c) Improving the orthodontic treatment process
During treatment, orthodontists annotate skull X-rays with landmark points from which clinically useful measurements of angles and lengths are taken. Historically, this manual annotation process is time-consuming for each patient. Drawing on the statistical shape modelling research [1-3], and its application to skulls [5], UoM developed a fully automatic system which can locate 54 important landmark points within a few seconds. This system was licensed to Audax (a medical software company) in 2017, who integrated it into their software for orthodontists, AudaxCeph, as an optional module called TINA (Tracing Is Now Automatic) [D].

It is estimated that each orthodontist sees 200-400 new patients a year, leading to a saving of 16-33hrs/year per orthodontist. Overall the system has so far saved 2-4 years of orthodontist time and reduced inconsistencies in measurements caused by differences in performance of orthodontists [E]. As of December 2020, since 2017 over 933 licences have been sold in over 80 countries worldwide [D].

Audax have confirmed that "*Based on positive feedback from our users and the increasing importance of an automatic tracing feature, we renewed the license agreement in August 2019 for another 5 years. TINA is now included as an integrated standard module in our AudaxCeph packages*" [D].

(ii) Improving animal welfare through automated joint disease detection

Poultry breeding programs use a balance breeding goal including components of production, product quality welfare, health and reproductive fitness. Leg health assessment is a crucial step in genetic selection whereas selection candidates with either clinical or sub-clinical leg health issues are not used for breeding. Tibial Dyschondroplasia (TD) is a leg-joint disease, a condition in which there is substitution of bone for cartilage in the tibia at the knee, and can manifest both clinically and sub-clinically, with the latter being very difficult to detect. As part of its breeding policy, for the last 30 years Aviagen – a world-leading poultry breeding company supplying breeding stock to customers in 130 countries – would remove any birds with either clinical or sub-clinical TD (as identified with a hand held X-ray device) from its breeding programme. Aviagen also takes 3D X-ray CT images of all birds at particular ages in order to estimate meat yield to inform its breeding strategies.

In 2016, Aviagen approached Cootes to help identify TD using the routinely collected X-ray CT images. Using the RFRV-CLM algorithm [4], Cootes built a software system that automatically locates the joints, and identifies those birds affected by the disease. Following their evaluation of the software in 2017, Aviagen signed a licence to use it in all their breeding sites.

The system is now installed in their breeding sites in the UK and US. It analyses about 12,000 birds a week. It has enabled the company to move to a more accurate and higher throughput way of assessing clinical and sub-clinical leg health. Aviagen have confirmed that compared to using the hand-held device, the UoM-developed system enables better accuracy and reduces the amount of bird handling involved [F]. They state *"The system's more accurate methods to assess skeletal integrity in the live birds allows us to select for biological performance (e.g., feed efficiency and yield) while maintaining and improving skeletal support which is essential as it will contribute positively to bird welfare and liveability"* [F]. As a result, the Aviagen birds are *"recognised in the industry globally as being much better in terms of leg health when compared to competitors and the UoM system enables us to keep our competitive advantage"* [F].

5. Sources to corroborate the impact

[A] Letter of support from Director, Imorphics Ltd, January 2020
[B] Imorphics Accounts, Companies House, 2016
[C] Letter of support from CEO Visiana, February 2021
[D] Letter of Support from Managing Director, Audax d.o.o, December 2020.
[E] Independent testimonial of Audax system by Luis Huanca (Independent Swiss Orthodontist) "*The fastest tracing in the world?"* [Online Blog dated 1 May 2018]
[F] Letter of support from Director of Global Genetics, Aviagen, June 2020