Institution: Keele University

Unit of Assessment: B11 Computer Science and Informatics

Title of case study: Automated object recognition and focussing for Medical Applications

1. Summary of the impact

This Keele University research in multiscale object recognition has led to two key breakthroughs: (a) the automated identification of tissue boundaries in computer tomographic (CT) scans, enabling the latest radiotherapy equipment to more accurately target diseased tissue thus avoiding neighbouring healthy organs. Such improvements are essential to the successful roll-out of new more precise linear accelerators in the treatment of cancer; (b) new fractal algorithms to characterise the quality of transplanted cell growth from post-operative biopsies. By automating the selection of the healthiest cells this has assisted the generation of patient-specific cartilage and is essential for the development of a medical capability for large-scale patient-specific generation of cartilage growth for the treatment of arthritis. It has indirectly led to software improvements in cell-tracking and to achieving reliable auto-focussing in high throughput non-invasive microscopy.

2. Underpinning research

The University's Computational Intelligence and Cognitive Science group has undertaken a significant programme of research into computer vision for (i) the automated recognition of specific artefacts within medical images, (ii) the automated evaluation of these artefacts in terms of medically relevant criteria such as the extent of cell growth and differentiation, and (iii) an automated procedure for focussing the complex and expensive devices used to generate such images. In each of these three stages, the key idea is to assist or replace the domain-specific (medical) expert with automated techniques, such that the number of patients who can be diagnosed can be greatly increased and that the diagnosis and treatment for each patient can be more effective and safer. This has not previously been possible through conventional approaches to pattern recognition.

In the first stage (the automated recognition of specific artefacts within medical images) the *multiscale* formalism [1] was used to develop new *component analysis* algorithms. This work demonstrated that such algorithms can match the performance of a medical specialist in segmenting images by organ and tissue type, thereby locating and isolating the organs of interest [2].

In the second stage (the automated evaluation of these artefacts in terms of medically relevant criteria) these algorithms were extended to distinguish between high-quality and low-quality tissue growth (in the case of monitoring regeneration) [3] or between cancerous and non-cancerous tissue (in the case of monitoring deterioration) [2].

In the third stage these algorithms were used as an alternative to conventional Laplacian-based techniques to generate more accurate images and 3D measurements of cells within a laboratory culture, by extracting patterns revealed at different depths and locations. This has led to a demonstrably improved auto-focus method, such that cells can now be automatically tracked over extended periods (weeks) with markedly improved image quality: a revolution for medical laboratories [4,5]. The auto-focusing methods also permits the construction of "2.5D" images of the cell cultures, which further assist in long-term cell tracking (BBSRC award 1.2013-12.2016).

Key researchers:
Dr K P Lam (lecturer, 1995-ongoing)
Mr D Collins (lecturer, 1987-ongoing)
Dr C Day (lecturer, 2001-ongoing)
Dr J Austin (postdoctoral research assistant, 1996-ongoing)

3. References to the research

The following are peer-reviewed international conference papers and journal articles.

[1] KP Lam, JC Austin and CR Day (2007*). A coarse-grained spectral signature generator*. Proc. Eighth International Conference on Quality Control by Artificial Vision, SPIE vol. 6356, 63560S. doi:10.1117/12.736723

[2] KP Lam, DJ Collins, J Sule-Suso, R Bhana and A Moloney (2013). *On Evaluation of a Multiscale-based CT Image Analysis and Visualisation Algorithm*. Proc. IEEE Sixth International Conference on Biomedical Engineering and Informatics (BMEI), December 2013.

Note, regarding the timeline, that this publication is preceded by two poster presentations, at (i) IEEE Thirteenth International Conference on Information Visualisation (IEEE/IV09), Barcelona, July 2009 (KP Lam, DC Collins, J Sule´-Suso and R Bhana: *ACTIVE - Advanced CT Image Visualisation Environment*) and (ii) European Multidisciplinary Cancer Congress on Integrating Basic and Translational Science, Surgery, Radiotherapy, Medical oncology, Advocacy and Care, Stockholm, September 2011 (J. Sule-Suso, KP Lam, R. Bhana, F Adab, S. Sargeant, DJ Collins, A Patel, A Moloney: *Three-Dimensional Imaging for Radiotherapy Planning in Prostate Cancer*), which also appeared as a supplement in European Journal of Cancer 47: S194, 2011, doi:10.1016/S0959-8049(11)70976-5.

[3] KP Lam, DJ Collins and JB Richardson (2013). *FACE: Fractal Analysis in Cell Engineering*. Proc. IEEE International Joint Conferences on Computer, Information, and Systems Sciences, and Engineering (CISSE 2011; Springer Lecture Notes in Electrical Engineering Volume 152: Innovations and Advances in Computer, Information, Systems Sciences, and Engineering), pp 1151-1164. doi: 10.1007/978-1-4614-3535-8_95

[4] WA Smith, KP Lam, Collins D and J Tarvainen (2013). *Estimation of Depth Map using Image Focus: A Scale-Space Approach for Shape Recovery*. Proc. IEEE International Joint Conferences on Computer, Information, and Systems Sciences, and Engineering (CISSE 2010; Springer Lecture Notes in Electrical Engineering Volume 151: Emerging Trends in Computing, Informatics, Systems Sciences, and Engineering), pp 1079-1090. doi:10.1007/978-1-4614-3558-7_92 (Also in REF2)

[5] KP Lam, KT Wright, KP Dempsey & WA Smith (2013). *A Computational Approach to Quantifying Axon Regeneration in the Presence of Mesenchymal Stem Cells*. Proc. IEEE Sixth International Engineering in Medicine and Biology Society (EMBS) Conference on Neural Engineering, November 2013.

Grants

EPSRC 26/09/2005-25/09/2007 £331,158
EP/C008138/1 Element-Specific X-ray Imaging for Security Applications
Investigators: PW Haycock, KP Lam, CR Day and AT Kearon
Partners: The Forensic Science Service, X-Tek Systems Ltd

BBSRC 01/2013-12/2016 £92,173
BB/J012998/1 Spatiotemporal Biometrics for Stem Cell Specific Cellomics
Investigators: KP Lam, JB Richardson and J Spencer-Fry (Industry Supervisor)

4. Details of the impact

In 2000 the National Cancer Plan was developed to address the problem of poor UK cancer survival rates. A major part of the subsequent reform was the national upgrade in radiotherapy linear accelerator provision: the machines that are used to kill cancer cells by damaging their DNA but which, ahead of this upgrade, used low-accuracy high-energy radiation that tended to damage neighbouring healthy cells as well as cancer cells. Ultimately the new machines will be rolled out into every cancer treatment centre in the UK. These new machines provide significantly higher resolution radiation targeting of malignant tumours, with multiple low-power beams focusing on the target tumour, providing a high dose where the beams converge but only a low dose along the path of individual beams, thus minimising damage to healthy tissue near the tumour. It is therefore essential that the introduction of these new machines is accompanied by new equally-accurate localisation algorithms for the processing of the corresponding CT scans, in order to direct the targeting at the diseased tissues rather than neighbouring healthy organs.

Ultimately this technology will apply to all cancers but the focus for the impact of the first stage of the research outlined in section 2 was to apply it to prostate cancer - the third biggest killer, behind lung and breast cancer, and the hardest to diagnose and target. Keele's Computer Science (CS) researchers applied the research outputs from stage one to this problem by working with the team of oncologists, radiologists and radiation physicists at the new state-of-the-art Cancer Centre at the University Hospital of North Staffordshire (UHNS, NHS Foundation Trust). The UHNS team provided raw volumetric CT scan sets from patient data, which the CS researchers processed using the new multiscale algorithms. The algorithms were judged by the team of specialists to be able to produce consistently correct identification of tissue boundaries (and so tumour location for targeting) even where the team themselves had produced different boundary identifications on separate attempts to delineate the same tissue [2]. This has led to a 50-patient clinical trial, which started in summer 2011 and has to date (with circa 70% completion) produced very promising results. As a secondary benefit (explored in a related clinical trial) patients are being shown the output boundaries (in 3D) from the algorithms superimposed on the raw CT scans in order to best depict the levels of certainty and uncertainty involved and so fully involve them in the decision making process. This related clinical trial was completed in 2012 and the facility is now part of the cancer treatment service (*Radiotherapy Brachytherapy*) available to patients; see section 5 for online reference.

The Robert Jones and Agnes Hunt Orthopaedic Hospital at Oswestry (RJAH, NHS Foundation Trust) has used cell therapy (tissue engineering) to treat patients with cartilage injuries and associated diseases (including arthritis) for over a decade, by transplanting cells that make new cartilage to replace that which is damaged or missing.

Based on the second stage of the research outlined in section 2 above, RJAH provided historical sets of biopsy images from patients with varying degrees of successful cartilage growth. The historical assessment of quality has involved invasive surgical techniques, is extremely slow, lacks objectivity, is costly, and is above all liable to human error. The CS researchers applied their new multiscale fractal algorithms to characterise the quality of transplanted cartilage cell growth from post-operative biopsies, producing a quantitative measure of cell quality that matched the assessment of domain experts [3]. By then applying similar algorithms to assess cartilage growth

in live cell laboratory based cultures (currently a highly labour intensive process), the aim is now to develop large-scale yet patient-specific cartilage generation capability. A three-way MRC-funded clinical trial has received ethical approval and is now underway.

To facilitate in vitro measurement of stem cell culture development over an extended period (weeks), it is necessary not only to have algorithms to produce the above measurements, but also to accurately track and focus on target cells non-invasively. The conventional Laplacian-based techniques for this were known to be inaccurate. The CS researchers developed their new algorithms to improve not just the tracking of cells but also the auto-focus method used by the high throughput 3D phase contrast microscopy platform. We are now working toward incorporating such improvements into the equipment of the company that produces this platform (CM Technologies Ltd, previously Chip-Man Technologies Ltd): see [5] and the BBSRC award in section 3.

5. Sources to corroborate the impact (indicative maximum of 10 references)

(Paragraph 1 of section 4 is introductory.)

Source to corroborate the impact in paragraph 2 of section 4:

- Ethics approval document for the "High Performance Interactive Visualisation for Patient Care" clinical trial at the University Hospital of North Staffordshire. Available on request.

  Clinical trial already ~70% complete, with very promising results. Initial results published in [2].

- The related trial (project VERT) was successfully completed in Nov. 2012; the work has led to new procedure evident online at:

  http://www.mycancertreatment.nhs.uk/treatment/single_report.php?hospital=UNIVERSITY%20HOSPITAL%20OF%20NORTH%20STAFFORDSHIRE&trust=UNIVERSITY%20HOSPITAL%20OF%20NORTH%20STAFFORDSHIRE%20NHS%20TRUST&service=Radiotherapy%20Brachytherapy&siteCode=RJEHQ&sctcode=11-3T-4&teamid=185&type=pdf

- Lead Oncologist, Cancer Centre, City General Hospital, University Hospital of North Staffordshire

(Paragraph 3 of section 4 is introductory.)

Source to corroborate the impact in paragraphs 4 and 5 of section 4:

- Ethics approval document for the three-way clinical trial at The Robert Jones and Agnes Hunt Orthopaedic Hospital at Oswestry. Available on request.

- Consultant Orthopaedic Surgeon, Institute of Orthopaedics, The Robert Jones & Agnes Hunt Orthopaedic Hospital NHS Foundation Trust