Institution: King's College London

Unit of Assessment: UoA15 – General Engineering

Title of case study: Robust and Accurate 2D-3D Image Registration

1. Summary of the impact

A collaborative research project between the Division of Imaging Sciences and Biomedical Engineering, King's College London (KCL) and Philips Healthcare has devised methods to register (i.e. align or match) pre-operative 3D computed tomography (CT) images to intraoperative 2D X-ray images, resulting in more accurate and robust registration/alignment measures. The measures can be applied directly to images from standard X-ray machines, allowing for rapid translation to guide surgical procedures and radiotherapy. These measures (or close variants) are used routinely in commercial products by Accuray, Philips Healthcare and Cydar Ltd (KCL spinout), benefitting the care of hundreds of patients worldwide, every day.

2. Underpinning research

The process of 'image registration' allows information to be transferred between different medical images. At the core of any registration/alignment system is the similarity measure that determines when the images are accurately matched. A measure that performs poorly can result in alignment errors and information can be transferred to the wrong position, with potentially serious clinical consequences for the patient. In 2D-3D image registration, one image is three-dimensional (e.g. a CT image) and another is two-dimensional (e.g. an X-ray image). The registration process allows information available in a high quality 3D CT image to be used directly in situations where CT scanning is not appropriate but where X-ray imaging is. For instance, in X-ray-guided, minimally invasive surgery where surgeons plan on a preoperative 3D CT image but where during the operation only real-time 2D X-rays are available.

The Division of Imaging Sciences and Biomedical Engineering at KCL has helped devise methods to align 3D CT images to 2D X-ray images. The principal KCL researchers involved in this work are Hawkes (1989-2004, Senior Lecturer and subsequently Professor), Hill (1989-2004, Lecturer and subsequently Professor), Penney (1995-2003 and 2007-present, PhD Student, Research Fellow and subsequently Senior Lecturer) and Rhode (2001-present, Research Fellow and subsequently Senior Lecturer). Previous, 'feature-based' methods required the difficult extraction of specific features (e.g. blood vessel outline) from the 3D and 2D images before registration. This is very difficult to achieve accurately and robustly using clinical images and has limited the clinical adoption of such methods. An alternative, 'intensity-based' approach matches images on raw image intensity values. Prior to 1995 only one such 2D-3D method has been published and this required two calibrated X-ray images, which were not available from standard equipment.

Since 1995 a collaborative research program between KCL and Philips Healthcare produced two new similarity measures, namely pattern intensity and gradient difference [1-3], which have high accuracy and robustness. The measures are designed specifically to work with real data, being invariant to a number of differences between CT and X-ray images which caused low robustness in measures used previously. KCL researchers clearly demonstrated this by testing their measures against known phantom gold-standard measurements and against the performance of other measures [1]. Increasingly realistic data was used to show accurate (sub mm errors) and robust performance: firstly to phantom data digitally enhanced with clinical features [1]; and then to routinely acquired clinical data [2]. More recently [5] reports the use of these measures in a series of 23 operations at KCL.

Work at KCL, again in collaboration with Philips Healthcare, pioneered the use of these measures to track a trans-oesophageal echocardiography (TOE) probe in X-ray images [5]. Our first-in-man study [6] demonstrated the combined use of these two very complementary imaging modalities: TOE providing 3D soft tissue anatomy and X-ray providing accurate instrument position.

The measures are patent protected [3] in the US, Japan and Germany and have been referenced by 23 subsequent patents filed by major imaging and image-guided surgery companies, including

Siemens, GE, Toshiba and Medtronic.

3. References to the research

(1) Penney GP, Weese J, Little JA, Desmedt P, Hill DL, Hawkes DJ. A comparison of similarity measures for use in 2-D-3-D medical image registration. IEEE Trans Med Imaging 1998;17(4):586-95. Doi: 10.1109/42.730403

(2) Penney GP, Batchelor PG, Hill DL, Hawkes DJ, Weese J. Validation of a two- to three-dimensional registration algorithm for aligning preoperative CT images and intraoperative fluoroscopy images. Med Phys 2001;28(6):1024-32. Doi: http://dx.doi.org/10.1118/1.1373400

(3) Weese J, Buzug T, Penney GP, Hawkes DJ. Method of determining the transformation between an object and its three-dimensional representation and device for carrying out the method. US Philips Corporation. Patent US 6144759. Published: 7.11.2000. http://www.google.com/patents/US6144759?cl=en

(4) Penney G, Varnavas A, Dastur N and Carrell T. An image-guided surgery system to aid endovascular treatment of complex aortic aneurysms: description of initial clinical experience. In proc. Image Processing and Computer Assisted Intervention 2011, pp 13-24.

(5) Gao G, Penney G, Ma Y, Gogin N, Cathier P, Arujuna A, Morton G, Caulfield D, Gill J, Aldo Rinaldi C, Hancock J, Redwood S, Thomas M, Razavi R, Gijsbers G, Rhode K. Med Image Anal 2012;16(1):38-49. Doi: 10.1016/j.media.2011.05.003

(6) Housden RJ, Arujuna A, Ma Y, Nijhof N, Gijsbers G, Bullens R, O'Neill M, Cooklin M, Rinaldi CA, Gill J, Kapetanakis S, Hancock J, Thomas M, Razavi R, Rhode KS. Evaluation of a real-time hybrid three-dimensional echo and X-ray imaging system for guidance of cardiac catheterisation procedures. Med Image Comput Comput Assist Interv. 2012;15(Pt 2):25-32.

4. Details of the impact

Similarity measures developed by the Division of Imaging Science & Biomedical Engineering at KCL have either been directly used or have very strongly influenced commercial systems by Accuray Inc (Cyberknife), Philips Healthcare (Echo Navigator) and Cydar Ltd (a KCL spinout company). These systems use 2D-3D image registration to transfer information between medical images. This information is then used to guide surgical treatment or radiotherapy. It is therefore extremely important, for long and short-term patient care, that the information is transferred accurately and robustly.

Accuray CyberKnife

The CyberKnife is a state-of-the-art radiosurgery system, delivering high-energy radiation to patients based on a treatment plan devised from a pre-operative 3D CT. It is manufactured by the US company Accuray Inc and while first developed in the early 1990's, it is being continually developed, with a new version - the CyberKnife M6 System - released in 2013. Accurate guidance is achieved by registering the 3D plan to 2D X-ray images acquired from the patient during treatment. The robot follows the treatment plan, and due to regular 2D-3D registrations, radiation can be accurately delivered even if patient movement occurs. KCL research has strongly influenced the registration similarity measures used by Accuray, who state that our developed measures, "pattern intensity and gradient difference have proved to be the most efficient and robust methods, a conclusion also verified by our (i.e. Accuray's) work" [7a] (which cites Penney et al. 1998 and 2001). The publication and subsequent Accuray patent [7b] (which also cites Penney et al. 1998 and 2001) describe a similarity measure that is extremely similar to (approximately a hybrid between) the pattern intensity and gradient difference measures.

The CyberKnife system uses this similarity measure to link the treatment plan to a radiation

delivery system for intracranial targets (6D skull tracking) [7a] and spinal tumours (Xsight spine tracking) (7c, which cites Penney et al. 1998 and 2001; and refers to the similarity measure as "pattern intensity"), ensuring that the radiation is delivered to the patients according to the treatment plan. As of 2010, 90,000 patients had been treated with the CyberKnife system [7d] - a large percentage of which would have had their radiation treatment guided using a derivative of the similarity measure developed at KCL. There are 272 CyberKnife centres worldwide, five in the UK, one of which is at the Royal Marsden, who describe how a great many of the benefits of the CyberKnife can be attributed to its accuracy, a major component of which is the registration similarity measure [7e].

Philips Healthcare

After the KCL first-in-man clinical study in partnership with the Department of Cardiology at Guy's and St. Thomas' NHS Foundation trust (Housden et al. 2012), Philips released a robust clinical prototype to other international partner sites (University of Colorado Hospital, University Hospital Zurich and Lenox Hill Hospital New York) to perform a larger clinical study. In October 2012 a commercial product allowing integration of real-time 3D trans-oesophageal echo imaging with real-time X-ray fluoroscopy (Echo Navigator) was released by Philips [8a]. FDA clearance was obtained for the Echo Navigator in March 2013. The attached letter from Philips Healthcare confirms the pioneering KCL research underpinning this product [8b].

Cydar Ltd image-guided surgery system

In 2009 consultant vascular surgeons, Mr Tom Carrell and Mr Bijan Modari, requested KCL expertise in providing additional guidance for a new procedure: complex endovascular aortic repair. KCL researchers developed an image-guided surgery system, using the previously KCL developed similarity measures (described in Penney 1998, 2001 and 2011), to overlay 3D information from the CT accurately onto the intraoperative 2D X-ray images. This system has helped treat over 100 patients at St Thomas' Hospital, London and continues to be in regular clinical use, leading to the formation of a KCL spin-out company, Cydar Ltd [9a], to translate this system into a clinical product. Two patents (which reference Penney 2011) filed by KCL are pending as International PCT Applications and have been licensed to Cydar Ltd.

Public dissemination

KCL's image guided surgery system was chosen to be one of the 24 exhibits at the week-long Royal Society Summer Science exhibition in 2011, an event that increases awareness, understanding and enthusiasm for UK science. This exhibition attracted over 14,000 visitors including school pupils, general public, media and Royal Society Fellows [10a]. The KCL system has also achieved widespread media attention through KCL's collaboration with Microsoft to design a touchless interaction interface based on the Microsoft Kinect gaming technology, with coverage on the national BBC news, Radio 4 (*Today* programme) and in New Scientist [10b].

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

7. Accuray CyberKnife

a) Fu D, Kuduvalli G. A fast, accurate and automatic 2D-3D image registration for image-guided cranial radiosurgery. Med Phys 2008;35(5):2180-194
b) Patent US 7480399 B2. Inventors: Fu D, Kuduvalli G. Apparatus and method for determining measure of similarity between images. Accuray, Inc. Patent. Publication date: 20.1.2009: http://www.google.co.uk/patents/US7480399
c) Ho AK, Fu D, Cotrutz C, Hancock SL, Chang SD, Gibbs IC, Maurer CR Jr, Adler JR Jr. Neurosurgery 2007;60(2 Suppl 1):ONS147-56; discussion ONS156. A study of the accuracy of cyberknife spinal radiosurgery using skeletal structure tracking. Doi: 10.1227/01.NEU.0000249248.55923.EC
d) Accuray Publication: Kilby W, Dooley JR, Kuduvalli G, Sayeh S, Maurer CR Jr. The CyberKnife Robotic Radiosurgery System in 2010. Technol Cancer Res Treat 2010;9(5):433-52: http://www.tcrt.org//mc_images/category/4309/02-kilby_tcrt_9_5.pdf
e) Royal Marsden CyberKnife brochure: http://www.royalmarsden.org/document.doc?id=7

8. Philips Healthcare: EchoNavigator
   a) EchoNavigator: http://www.healthcare.philips.com/main/products/interventional_xray/Product/interventional_cardiology/echonavigator/index.wpd
   b) Letter from Philips Healthcare on file and at: http://www.kcl.ac.uk/medicine/research/divisions/imaging/ref.aspx

9. Cydar Ltd image-guided surgery system
   a) Website: www.cydar.co.uk

10. Public dissemination
   a) Royal Society Summer Science exhibition: http://royalsociety.org/summer-science/2011/keyhole-surgery/
   b) New Scientist: Kinect imaging lets surgeons keep their focus. Published 17.5.2012: http://www.newscientist.com/article/mg21428655.200-kinect-imaging-lets-surgeons-keep-their-focus.html