GIFT Surg

# Guided Instrumentation for Fetal Therapy and Surgery

UCL

KU LEUVEN

Supported by wellcome trust

EPSRC Engineering and Physical Sciences Research Council

# Contents

# The birth of GIFT-Surg

**December 3rd, 2012**
Prof Neil Marlow introduces Prof Sebastien Ourselin to Prof Paolo de Coppi over a coffee. Prof de Coppi mentions “I have someone you have to meet”.

**December 15th, 2012**
Prof Paolo De Coppi introduces Prof Sebastien Ourselin to Prof Jan Deprest. Together they discuss how good it would be if they were able to apply the same detailed imaging techniques and minimally invasive tools used for other treatments, such as neurosurgery, in treating medical conditions of unborn babies.
It must be both minimally invasive and precise for the safety of the mother and the unborn child.

“We know the earlier the intervention the better the outcome.”

**July 3, 2013**
The Wellcome Trust and EPSRC announces the funding of the 7 year IEH grant: Image-Guided Intrauterine Minimally Invasive Fetal Diagnosis and Therapy.

**July 1st, 2014**
The project formally begins. Renamed GIFT-Surg (Guided Instrumentation for Fetal Therapy and Surgery)

**December 1st, 2014**
5 months in and the project consists of over 38 staff and PhD students in two countries working towards the common goal of developing safe and minimally invasive tools and therapies for the unborn child.

## Introduction

Performing surgery on fetuses whilst still in the womb is a risky business. Although pioneering work in this field began in the 1980s, it remains very challenging, with only a few highly trained teams around the world treating a handful of conditions. Our aim with GIFT-Surg is to create breakthrough transformations and improvements in the treatment of congenital problems in the womb.

- Around 1 in 100 babies are born with a severe birth defect
- Collectively these defects are estimated to be responsible for over 1/3 of all paediatric hospital admissions
- Up to half of the total cost of paediatric hospital treatment is towards this

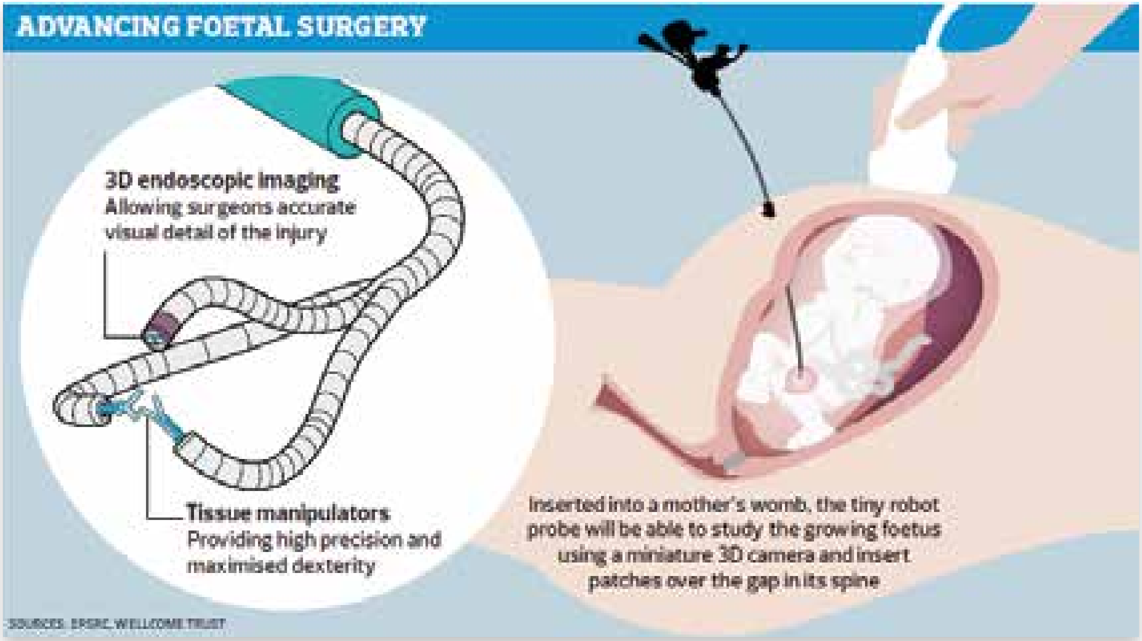

**Above:** Comparison of ultrasound scan and endoscopic footage of fetus in proposed GIFT-Surg software tool.

## Key Impacts

- Creation of flexible instruments that are designed to allow surgeons to perform minimally invasive surgery with improved safety and efficacy
- Allow surgeons to actively and reliably work in a fragile, complex and real-time environment
- Enable surgeons to better prepare for surgeries by providing more pre-operative data
- Provide clearer visualisations and greater scope of view for surgeons

## Flexible Actuated Surgical Device

GIFT-Surg is working to develop an extended flexible mechatronic multi-finger device that will be fed in through a small incision, of approximately 4mm, in the abdomen of the mother. This device will enable surgeons to operate and perform complex procedures from outside the womb. The three “fingers” of the device will offer the surgeon superior dexterity and better vision at the surgery site. While two of the fingers can carry out delicate procedures, in the case of spina bifida, patching up the source of the protrusion from the spine, the third will carry an innovative endoscopic imaging system that will create 3D images of the environment inside womb and acquire tissue properties making it possible to identify anatomic structures on and below the tissue surfaces. The surgeon will have direct and real-time access to these images and guidance cues which will be clearly displayed on a screen visible to them in the operating theatre. The images will also serve as a feedback for guiding the dexterous instrumentised arms.




This ensemble of technology could allow surgeons to perform fetal surgeries that are currently too risky for both the mother and unborn baby.

By passing tools through a small incision, surgeons minimise the risks of complications for the mother and fetus, notably preterm labour. There already exists some fetal surgery which takes advantage of this. Minimal access with laser coagulation, for example, is the current standard of care for treating twin-to-twin transfusion syndrome (TTTS) a condition where two identical twins share blood through the same placenta. While the donor twin is deprived of blood and can develop growth defects, the other twin is given too much blood and can suffer from heart failure. To correct this, surgeons currently operate using a fetoscope with a laser coagulator attached to it. This cauterises the blood vessels that link the blood circulation between the twins. Although this is a working solution, the existing tools lack flexibility and therefore, this kind of surgery is still quite complex and has limited possibilities when twins, triplets and the placenta are arranged in certain configurations.

**Above:** Picture of an exit procedure, a type of fetal surgery performed at the time of delivery. Credits: Francois Luks, MD, Public Domain

Minimally invasive surgery can also be currently used to stimulate lung growth in another condition called congenital diaphragmatic hernia. However a subsequent more invasive procedure called ex utero intrapartum treatment procedure, or “EXIT surgery”, might then be required at the time of the baby’s delivery.

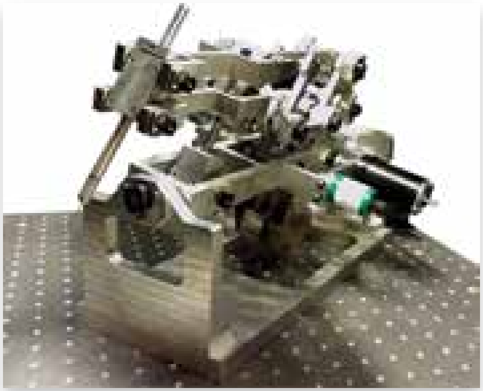
Even for spina bifida, a condition where there is an opening in the bottom of the spinal cord exposing nerves and veins, minimally invasive repair is possible in a few cases but it remains inaccurate, has a high failure rate and requires multiple small incisions, which increases the risks associated with the procedure. Although spina bifida is one of the most common birth defects, it also requires one of the most complex procedures for treatment.

As part of the project we aim to have flexible instruments that are designed to allow surgeons to perform minimally invasive surgery with increased efficacy and reduced complications for the unborn child.

## Latest Technological Developments

We will build on the latest developments in sensing, actuation and mechatronics.

Dedicated actuators or “stabilisers” based on fluidic muscles will be developed and integrated. These actuators will help create smooth and dynamic movement yet occupy much smaller footprints than standard approaches. This key aspect of the flowing and stabilising nature of the actuation mechanism is important, not only because it will be advantageous for safety purposes, effectively limiting the risk and impact of collisions and subsequent tissue damage, it will also allow surgeons to adjust better with the variable living nature of the mother and unborn child, reducing trauma and the risk for premature birth, compared to purely manual interventions. Although we do not intend to make the actuated arm fully automated or robotic, by using image guidance, advanced control approaches will be explored that intelligently assist the surgeon during the procedure. The design will, for example, help lessen tremors in the surgeon’s hand and allow for bigger or more fine-grained manipulation by scaling down the surgeon’s gestures.



**Above:** View upon stabilizer designed for ophthalmological micro-surgery – KUL technology which is made available for GIFT-Surg.

**Above:** Fetoscopic image of the tissue and veins of a fetus within the womb.

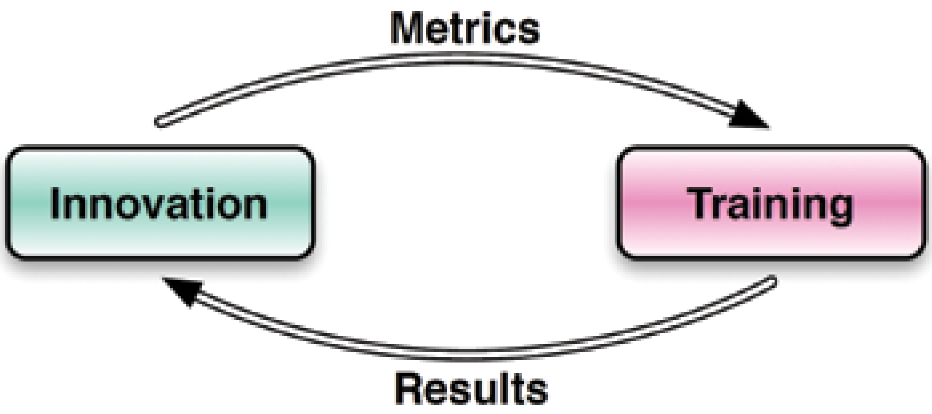
The 3D imaging probes will provide visualisation of tissue from inside the womb. Photoacoustic imaging probes will deliver harmless laser pulses to tissue. These light pulses will be absorbed by tissue and converted into ultrasound waves that will be received and processed to generate images. Optical ultrasound imaging probes will deliver light pulses to an absorbing nano-composite material to generate ultrasound. With both probe types, ultrasound waves will be received optically. Taken together, these 3D imaging probes will provide unprecedented functional and microstructural visualisations of the fetus and its environment.

In addition to 3D imaging and advanced and flexible tools, surgeons will be able to use external 3D ultrasonography as well as MRI, when available, to construct a plan for the operation based on the specific anatomy and pathology of the fetus to be operated on. Computer modelling embedded with biomechanical information will be able to compute and predict deformations that may occur during surgery. Both the pre-operative data and the feedback from the "live" 3D imaging will be fed into the model and processed to give surgeons ongoing context, much like a GPS might tell us where we are on a predefined map. Ultrasonic tracking of needles and probes will be provided using integrated miniature fibre optic ultrasound receivers.

**Above:** View on a dual-segment fluidic-actuated instrument. The compliant nature of this actuator is well suited for operating in a fragile environment.

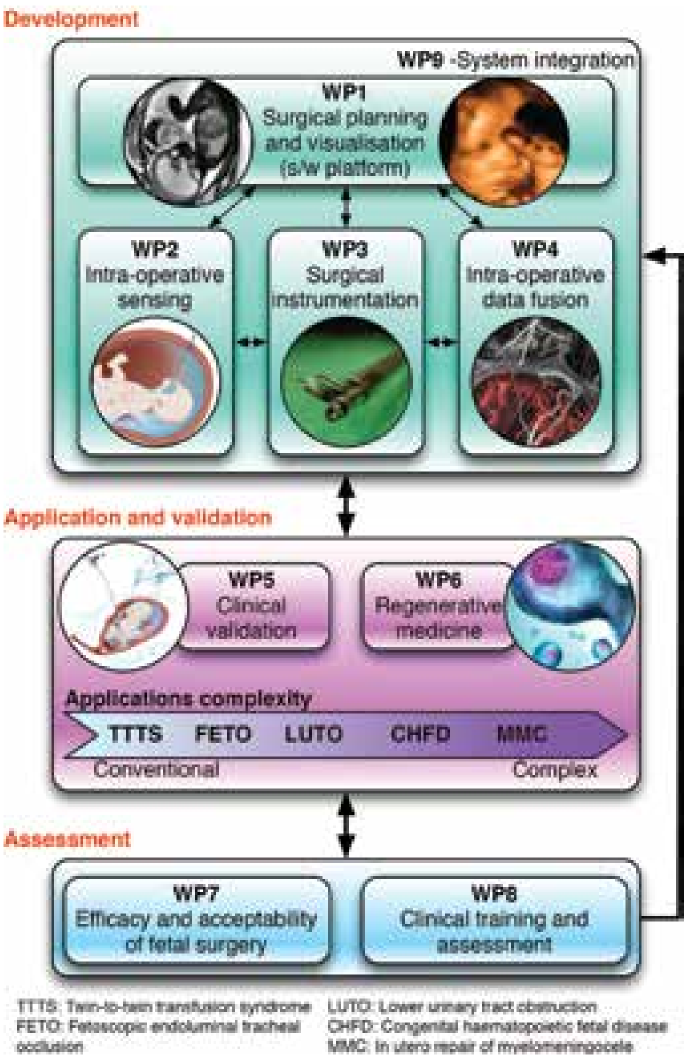
**Above:** How the 3D ultrasonography will be used along with the photoacoustic 3D tool.

As part of the program we will also be providing state of the art training to surgeons and clinicians on the tools and devices. There will be a series of technological assessments using life-like phantoms and metrics for objective skill analysis. Processes and training will be continuously evaluated to ensure the optimum methods of training are being used.




**By combining the elements of instrumentation, imaging, clinical training and public engagement, GIFT-Surg aims to provide surgeons with tools to help to make fetal surgery much safer and more efficient. The surgeon will still be at the centre of the operation but will be able to rely on additional guidance, like you might get from power steering, collision detection and rear cameras in a modern car.**

**Severe congenital defects account for many baby deaths each year but many more could survive if help could be given in the womb. Instead of carrying out neonatal surgery when it may be too late, pioneering new technology will transform this field of surgery and provide better outcomes.**




# Workpackages

The project is broken into multiple work packages to help manage its delivery. The workpackages (WPs) are not in the order of which things are done but instead how similar tasks are grouped together. Items from each WP will be happening simultaneously with others. Although all WPs require experts from a number of different disciplinaries some WPs rely more heavily on specific skilled professionals.

WP1: **Surgical planning and visualisation** is the creation and development of the software that will run the hardware and imaging systems. It is reliant on software developers and medical imaging specialists.

WP2: **Intra-operative sensing** involves the physical building of the camera and development of the photoacoustics system that will be used on the new tool to create 3D images. Most of this work will be carried out by Medical Physicists and Medical Engineers.

WP3: **Surgical instrumentation** is about the creation of the new tool itself. The design incorporating the flexibility and small size needed, will be developed by experienced Medical Engineers.

WP4: **Intra-operative data fusion** is about linking the information provided from different channels in real-time during the procedure, for example by co-registering intra-operative ultrasound and preoperative MR.

WP5: **Clinical validation** relates to testing the technical achievements in a preclinical and eventually clinical environment. It relies heavily upon the skills of clinicians and surgeons.

WP6: **Regenerative medicine** is about using the steps accomplished in WP1-5 and applying it to the breakthrough improvements in regenerative medicine.

WP7: **Efficacy and Acceptability of Fetal surgery** is about the ethics and economics of fetal surgery. It relies on clinical consultants as well as medical economists, and the general public by way of patient groups.

WP8: **Clinical training and assessment** is about training and ensuring medical professionals have the proficiency to use the new systems and equipment safely and flawlessly.

WP9: **System Integration** will take place throughout the complete project. This is about linking up all the various software and hardware components and robustly testing them.

# Investigators

# Prof Sebastien Ourselin

UCL Professor of Medical Image Computing
Principle Investigator GIFT-Surg

Sebastien Ourselin is currently Director of the EPSRC Centre for Doctoral Training (CDT) in Medical Imaging, Head of the Translational Imaging Group (TIG) as part of the Centre for Medical Image Computing (CMIC), and Professor of Medical Image Computing at UCL. His core skills are in medical image analysis, software engineering, and translational medicine. He is best known for his work on image registration and segmentation, its exploitation for robust image-based biomarkers in neurological conditions, as well as for his development of image-guided surgery systems. His research is often collaborative, involving clinical and commercial partners.

Sebastien is leading the translational imaging research program between CMIC and the UCL Institute of Neurology, and has established in collaboration with Prof Nick Fox a new imaging unit at Queen Square to deliver engineering solutions for clinical trials. In collaboration with Prof John Duncan, he is also leading the development of an image-guided neurosurgery platform, which has already been deployed within the interventional MRI environment at Queen Square for temporal lobe epilepsy. This work built the foundation to expand the work into neurosurgical planning, currently funded under the Wellcome Trust and Department of Health HICF scheme. He is also leading the development of the open-source NifTK platform. Most of these activities are underpinning GIFT-Surg's technological foundations.

**GIFT-Surg focus:**

As Principle Investigator, Sebastien Ourselin has overall responsibility of the project delivery. GIFT-Surg is a complex multi-disciplinary project where not a single scientist would have the full expertise on every clinical or technical area. For that matter, he is fully supported by the co-investigators but also has a dedicated project manager (Jenny Nery) to provide appropriate daily support. Sebastien is also Chair of the Project Executive and Project Management Board creating an appropriate structure to focus this large initiative.

In addition, he is specifically involved in the research efforts under surgical planning and intra-operative data fusion.

Surgical planning consists of accurate and detailed anatomical and functional documentation of the fetal organs of interest, fetal position and localisation of the placenta to assist with optimal port placement and subsequent insertion of probes or instruments. Preoperative computation will also support intra-operative biomechanical model changes and direct optimal imaging planes for real-time modalities that may be used to update preoperative anatomical structures. Existing software platforms at CMIC will be used to support the segmentation, registration and processing of fetal MRI and US images used during the planning phase.

Intra-operative data fusion will provide real-time feedback during therapy based on a combination of direct vision via the fetoscope combined with novel intrauterine imaging devices and external ultrasound, fused with preoperative models. To fuse preoperative information to the intraoperative anatomy, biomechanical models, models, statistical shape models and motion modelling will be used to deform 3D structural anatomical models to the information acquired in *vivo*.

## Dr Danail Stoyanov

UCL Lecturer in Computer Science
UCL Technical Manager GIFT-Surg

Dan obtained a BEng degree from King's College London in 2001 and a PhD degree from Imperial College London in 2006 where he continued with his post-doctoral research. In 2009, he was awarded a Royal Academy of Engineering/EPSRC Research Fellowship which he held at the Hamlyn Centre for Robotic Surgery at Imperial College London and subsequently at the Centre for Medical Image Computing (CMIC) and the Department of Computer Science, University College London (UCL). Currently, he is a Lecturer in Computer Science at CMIC, UCL where he leads the Surgical Robot Vision Research Group. His main technical research interests are in surgical vision and the recovery of morphology and motion at the surgical site during minimally invasive robotic surgery using laparoscopic images. The clinical aims and applications of his research are in the improvement of surgical practice starting from the surgical training process and translating to building better surgical systems for control, imaging and navigation during robotic minimally invasive interventions. In GIFT-Surg Dr Stoyanov is coordinating the Scientific / Technical contributions from the University College London.

**GIFT-Surg focus:**

The primary sensors for guiding current fetal interventions are cameras which observe inside the womb through fetoscopes and ultrasound probes imaging through the abdominal wall and the placenta.

The role of Dan's team within the GIFT-Surg project is to develop the surgical vision algorithms processing fetoscopic images, in particular to recover the non-rigid structure and motion of the surgical site in real-time and track the position of the camera and the instruments.

This information is crucial for image guidance, for example by augmented reality overlay of ultrasound or preoperative models, where the co-registration of data needs frequent updates to align with the operating field.

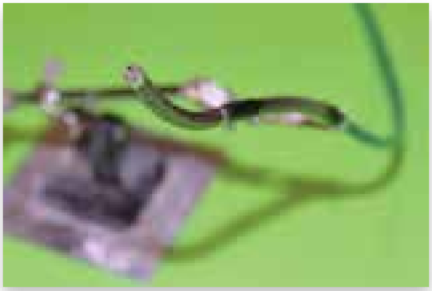
For active intraoperative guidance using imaging modalities like photoacoustics and forward facing ultrasound, vision algorithms can provide information to enhance the field of view and resolve image integration times. Information from the surgical site is also crucial for informing the mechatronic control systems of instruments using real-time measurements to facilitate precise and repeatable instrument-tissue manipulation and compensation of physiological motion.

In addition to surgical vision and assisting the imaging and guidance systems of GIFT-Surg, his team is leading the technical developments around understanding and quantifying surgical skills and competence, clinical workflow and system ergonomics. It is their particular interest to see how such quantitative metrics change and evolve as GIFT-Surg technology matures and provides exciting new capabilities to the clinical team.

## Dr Emmanuel Vander Poorten

KUL Technical Manager

Dr Emmanuel B. Vander Poorten received his degree in Mechanical Engineering in 2000 from the University of Leuven, Belgium. He obtained the title of Doctor in Engineering in May 2007, from Kyoto University, Japan. After obtaining the PhD, he returned to University of Leuven, where he is working as a postdoctoral researcher in the Mechanical Engineering Department. His research interests include surgical robotics, human-robot interaction, shared control, haptic interfacing, teleoperation control and development of intelligent instrumentation. Dr Vander Poorten is managing the activities of the Robot-Assisted Surgery group (www.mech.kuleuven.be /en/pma/research/ras). He has been coordinating FP7 projects RADHAR and SCATh on robotic wheelchairs and smart catheters respectively and is currently coordinating the FP7 project CASCADE on autonomous catheters for TAVI procedures and EurEyeCase, an H2020-project on robotic eye-surgery. In GIFT-Surg Dr Vander Poorten is coordinating the Scientific / Technical contributions from the University of Leuven.



**Above:** View on a dual-segment fluidic-actuated instrument. The compliant nature of this actuator is well suited for operating in a fragile environment.

**GIFT-Surg focus:**

Severe safety requirements, miniature access (with entry ports in the order of 3mm diameter) high dexterity, as well as the need to display superior manipulation and targeting precision in an extremely fragile and dynamic environment; GIFT-Surg has it all. Within GIFT-Surg the Leuven team will closely collaborate with the consortium and in particular the clinical partners in order to develop novel single- but also multi-arm instruments. Such instruments will be hinged within a dedicated stabiliser. The latter will reduce the surgeon's effort taking a part of the load for its account. Likewise, the stabiliser will facilitate the surgeon to operate in a tremor-free fashion. Emmanuel's personal interest lies in the design and control of the stabiliser and the compatible instruments. Not only do these devices need to cover a large workspace and move with great accuracy, they also need to be extremely responsive both to the surgeon and to the environment. Earlier experience in designing and controlling multi-DoF (multi-Degrees of Freedom) haptic interfaces and stabilisers will be helpful to meet higher-mentioned challenges.

Emmanuel will pay special attention to the development of compensation schemes that help limit the sheer stress applied upon the uterine wall and fetal membranes (Krupa et al. 2002) which might be responsible for a share of cases of premature birth. Experimental data gathered with this synergetic stabiliser will shed further new light upon the detailed tissue interaction and could also serve for analysis, training or guidance. This aspect also falls within Emmanuel's field of interest and he looks forward contributing to it. From earlier surgical robotic projects and spin-off activities it has been understood very well how important it is to continuously engage the surgeon in the process if one wants to develop true solutions to real problems. KUL will therefore collaborate closely with clinical colleagues on both sides of the Channel.

# Prof Simon Arridge

UCL Professor of Image Processing

Simon Arridge has been Professor of Image Processing in the Department of Computer Science, UCL, since 2001. He is also a visiting professor in the Department of Mathematics UCL, since 2011. He is Director of the UCL Centre for Inverse Problems which was opened in 2013. His research interests are in Inverse Problems with particular interest in Image Reconstruction in Medical Imaging. He has been a member of the editorial board of the Institute of Physics journal 'Inverse Problems' since 2000 and takes over as Editor-in-Chief in 2015. He is widely known for pioneering the development of Diffuse Optical Tomography which produces images of optical absorption and scattering parameters in tissue from measurements of transmitted or reflected light in the near-infrared part of the spectrum. He has developed extensive numerical modelling and image reconstruction tools for optical imaging which are widely used in the community. He has a strong interest in multimodal and coupled-Physics imaging techniques, including PET-MRI, PhotoAcoustics and Ultrasound Modulated Optical Tomography, amongst others.

**GIFT-Surg focus:**

PhotoAcoustic Tomography (PAT) is capable of producing very high resolution multispectral images of optical parameters several centimeters inside tissues. It is currently too slow to use in real time because of a trade-off in resolution and signal-to-noise ratio. A technique was recently patented for significantly accelerating this methodology using a combination of compressed sensing and time-series analysis methods. The enabling technology is the use of a spatial light modulator to acquire patterns of signals rather than pointwise samples. Simon is developing these ideas within a separately funded EPSRC project and will bring them into the foetal-surgery project as the ability to image endoscopically becomes developed. He aims to obtain realtime images in 3D with multispectral facility.

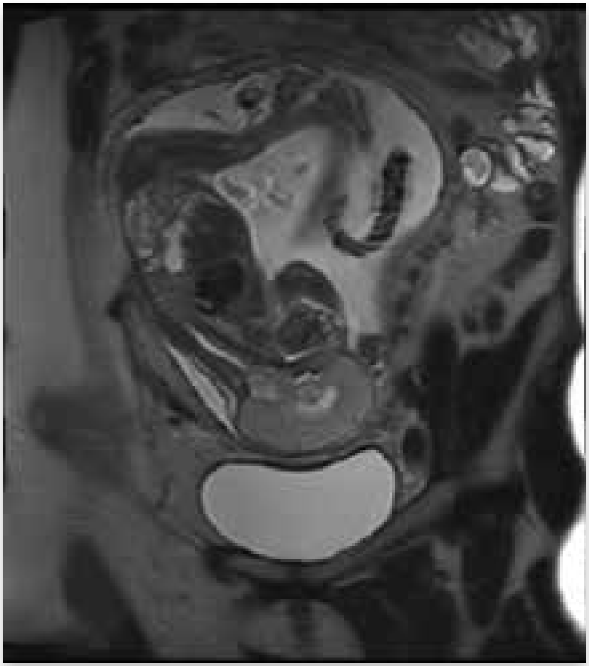
# Dr David Atkinson

UCL Senior Lecturer in MRI

David Atkinson is a Senior Lecturer in Magnetic Resonance Imaging (MRI) within the UCL Centre for Medical Imaging. His areas of expertise are in MRI acquisition and processing, especially in relation to clinical imaging research. He is an investigator on grants related to diffusion imaging outside of the head, “intelligent imaging”, cancer studies and imaging for fetal surgery.

**GIFT-Surg focus:**

Within the GIFT-Surg project, David will be providing MR images to support the planning of fetal surgery and studies examining the structure and health of the placenta.

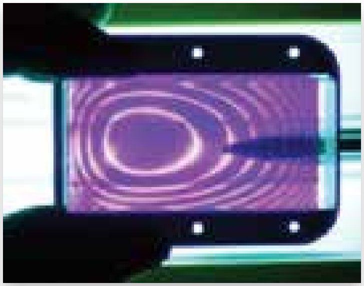


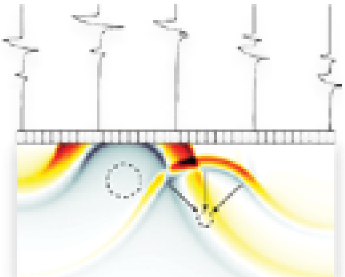
**Above:** MRI capture of 12-15 week old fetus

## Prof Paul Beard

UCL Professor of Biomedical Photoacoustics

Paul Beard is Professor of Biomedical Photoacoustics at UCL and holds an EPSRC Leadership Fellowship. He obtained a BSc in Physics at UCL. Following a period at Marconi Underwater Systems Ltd he returned to UCL and obtained a PhD in 1996 in Medical Physics. In 2003 he founded the Photoacoustic Imaging Group in the Department of Medical Physics and Biomedical Engineering. With more than 25 researchers it is now one of the largest groups worldwide in the field with specific expertise in photoacoustic instrumentation, image reconstruction algorithms, quantitative spectroscopic methods and the preclinical and clinical application of the technique.





**Above:** Thin film Fabry Perot ultrasound sensor.
**Below:** Photoacoustic image reconstruction using time-reversal.

**GIFT-Surg focus:**

A key objective of GIFT-Surg is the development of a novel intraoperative imaging platform based on photoacoustic (PA) imaging and laser generated ultrasound (US) for visualising fetal and maternal anatomy and function. PA imaging provides absorption based optical contrast making it well suited to visualising vascular architectures, while ultrasound provides complementary high resolution structural information based on mechanical contrast. This dual modality approach could be used, for example, to help identify anastomosing vessels during twin-to-twin transfusion syndrome surgery with PA imaging providing a map of the placental vascular anatomy set against the surrounding tissue morphology revealed by US. The broad objective is to develop a multi-modal platform that will provide co-registered 3D PA-US images over two different spatial scales; a high resolution image over a small field of view obtained using a miniature endoscopic device and a larger scale image obtained using a non invasive external imaging head.

A specific challenge that is the focus of current efforts relates to the development of the endoscopic imaging implementation. This requires a miniature ultrasonic detector array located at the tip of a flexible probe in order to record the PA and US signals used to form the image. Conventional thinking dictates using an array of discretely fabricated piezoelectric detectors but achieving the required level of miniaturisation and wideband acoustic performance is extremely challenging. We are exploring an entirely different approach that employs a thin film optical sensor based on a Fabry Perot interferometer formed by vacuum deposition methods. This offers new opportunities to realise devices with an unprecedented level of miniaturisation since the sensor can be formed on almost arbitrarily small substrates: for example, we have previously deposited one on to the tip of an 80μm diameter optical fibre. The technology is highly versatile and is being exploited to develop a range of devices that will fulfil a variety of imaging and detection roles within the project. These include a forward-viewing endoscopic fetal PA-US imaging probe that comprises a flexible fibre bundle with the sensor deposited at the tip to realise a 2D detector array. Highly miniaturised single element probes are also being developed for implementations where the PA or US image is formed by mechanical scanning or as miniature receivers for ultrasonic tracking of endoscopic devices for image registration purposes.

# Dr Anna David

## Reader/Associate Professor and Hon Consultant in Obstetrics and Maternal Fetal Medicine

Anna David is Reader/Associate Professor and Honorary Consultant in Obstetrics and Maternal Fetal Medicine at Institute for Women's Health, University College London (UCL), London. She qualified from St Andrew's University in Scotland and Manchester University in England, and did specialty training in obstetrics and gynaecology in London. At University College London (UCL) Anna completed her PhD on fetal gene therapy in 2005, and then undertook subspecialty training in maternal fetal medicine at UCLHospital. She was awarded a UK National Institute for Health Research (NIHR) Senior Lectureship in Women's Health in 2008, when she also became a consultant.  She was promoted to Reader in 2012. She has a clinical practice at UCLH in fetal medicine, fetal therapy and obstetrics. Her main research is in translational medicine. She leads the Prenatal Cell and Gene Therapy Research Group at UCL Institute for Women's Health whose aim is to develop prenatal therapies for life-threatening disorders such as congenital diseases and obstetric complications.

**GIFT-Surg focus:**

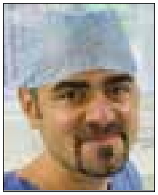
Improving visualization and safe access to the fetus are key to the development of the innovative therapies that are poised to transform prenatal therapy. These include stem cell transplantation and gene therapies to cure genetic disease, and regenerative medicine techniques to repair structural abnormalities. Evaluating the efficacy and acceptability of these new developments in fetal surgery will also be an important part of translating them into clinical practice.

Anna's role in the project is in two areas of work. The first workpackage uses breakthrough improvements in regenerative medicine. The research will test the feasibility and efficacy of the prenatal interventions optimised during the project for the management of two particular types of fetal abnormality: congenital fetal blood disorders such as thalassaemia, and in utero repair of spina bifida. Currently these conditions are either untreatable before birth (thalassaemia) or require highly invasive open fetal surgery (spina bifida).

The second workpackage will explore issues related to the practicalities of clinical translation. Ethical considerations in innovative fetal surgery will be addressed by firstly understanding the legal, ethical and moral framework in which clinicians and parents currently work, with assistance from Professor Richard Ashcroft, a leading bioethicist from Queen Mary University of London.

Anna will set up a Patient Public Involvement Advisory Group (PPIAG) to evaluate post-operative efficacy and patient acceptability of the project developments. This will include representatives from charities and parent groups linked with the fetal conditions to be treated. The PPIAG will work with the scientists and clinicians in GIFT-Surg to better understand the potential impact of the innovations in reality for fetal patients.

# Prof Paolo De Coppi



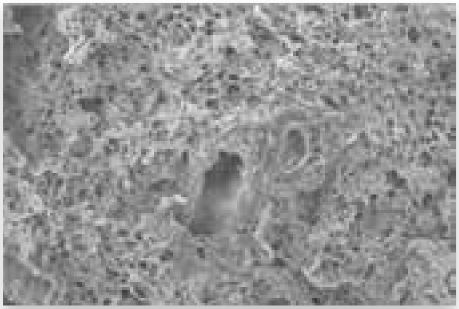
UCL/NIHR Professor of Paediatric Surgery
Great Ormond Street Hospital Consultant Paediatric Surgeon

Paolo De Coppi is the Professor of Paediatric Surgery and Head of Stem Cells and Regenerative Medicine Section, Developmental Biology & Cancer Programme at the UCL Institute of Child Health. He is also NIHR Professor and Consultant Paediatric Surgeon at the Great Ormond Street Hospital for Children and the UCL Institute of Child Health. Concomitantly he is an Professor at the University of Leuven, Belgium (since 2013), Adjunct Assistant Professor at the Wake Forest Institute for Regenerative Medicine, Wake Forest University, Wiston-Salem, NC, US (since 2009) and Honorary Assistant Professor Paediatric Surgery, University of Padua, Italy (since 2005).

**GIFT-Surg focus:**

Paolo has a special interest in congenital malformation and their treatment using minimally invasive techniques. He has focused his research interests on stem cells and tissue engineering, trying to find new modalities for the treatment of complex congenital anomalies. While working with Dr A. Atala at the Childrens' Hospital in Boston-US, he had the opportunity of identifying a new source of cells for therapeutic applications showing the possibility of using stem cells from amniotic fluid. This finding generated an international patent, the cover of the January 2007 issue of Nature Biotechnology, and it has opened the development of new ways for the correction of congenital malformations.

More recently, his team has demonstrated that these cells are able to differentiate into various tissues and to replace functional activity in animal models of diseases. He is now focused on developing reliable methods for stem cell isolation, expansion and differentiation at clinical level (GMP-grade). In 2010 he was part of the team, which performed the first successful transplantation of a tissue-engineered trachea on a child at the Great Ormond Street Hospital. Paolo is now working to translate these methods to fetal surgery, as well as providing surgical expertise on the project.



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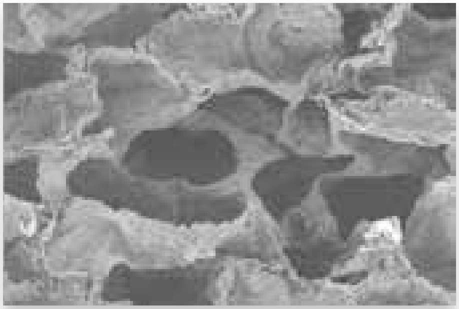
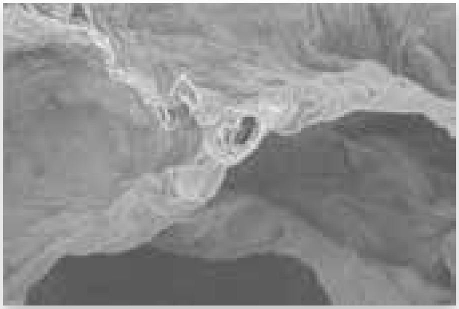


(B)



(C)

**Above:** Sheep lung after decellularization: cells can be washed out from the organs using detergents while maintaining their overall matrix structure
(A) At higher magnification it is possible to appreciate that both the acinar structure of the lung (B) is preserved together with the vessels which remain patent
(C) Maghsoudlou P, et al. Biomaterials. 2013 Sep;34(28):6638-48.

# Prof Jan Deprest

KUL Professor of Obstetrics and Gynaecology/UZ Leuven Consultant Obstetrician Gynaecologist

Jan Deprest is a Professor of Obstetrics and Gynaecology at the Katholieke Universiteit Leuven and Consultant Obstetrician Gynaecologist at the University Hospitals Leuven (Belgium). Prof Deprest is currently the academic chair of his department and the director of the Centre for Surgical Technologies at the Faculty of Medicine. He trained in fetal medicine in Leuven, St George's Hospital London (UK), Leiden (Holland) and attended the programme at Children's Hospital Philadelphia (PA, USA). He established the Eurofoetus consortium, which is dedicated to the development of instruments and techniques for minimally invasive fetal and placental surgery. The Leuven Fetal Medicine Team focusses on antenatal modulation of lung development, e.g. for pulmonary hypoplasia due to congenital diaphragmatic hernia as well as for bronchopulmonary dysplasia. He headed several clinical studies dedicated to the prenatal prediction of survival chances of fetuses with isolated CDH using genetic testing, ultrasound and fetal MRI. He developed a percutaneous method for fetoscopic placement of a balloon into the fetal trachea ("FETO"). In a European task force together with the University of Barcelona (Hospital Clinic) and London (King's College Hospital) could report on over 200 such procedures by 2009. This group now also conducts a world-wide randomized trial (www.totaltrial.eu). The group also researches the application of amniotic fluid derived stem cells for treating fetuses or neonates with CDH. Research into fetal membrane wound healing is ongoing, as the clinical problem of iatrogenic premature preterm rupture of the fetal membranes is not solved yet. More recently the group moved into open fetal surgery for spina bifida. The current project is dedicated to making this intervention less invasive.

**GIFT-Surg focus:**

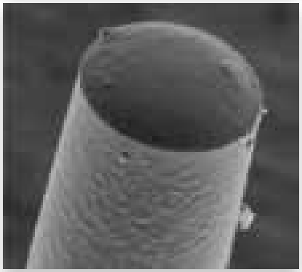
He and his colleague will participate in the project in different ways. As a clinical fetal surgery center with a large portfolio of procedures, they will bring in their experience as well as patient material. Close interaction with the engineers working on image analysis as well as instrument building will contribute to swift progress and problem solving. Also the group offers the opportunity for testing innovation in the safe setting of the experimental surgical lab, prior to move to clinical application.

**Above:** Clinical surgery at University Hospitals Leuven

# Dr Adrien Desjardins

UCL Senior Research Fellow and Lecturer

Dr Adrien Desjardins is a Lecturer and Senior Research Fellow in the Department of Medical Physics and Biomedical Engineering. He obtained his PhD from Harvard and from the Harvard-MIT Health Sciences and Technology Programme. Prior to joining UCL, he was a Senior Scientist at Philips Research in the Minimally Invasive Healthcare Department. He leads a translational research programme that is centred on the development of medical devices and medical imaging platforms for guiding minimally invasive procedures. He has particular interests in optical, ultrasound, and photoacoustic imaging to provide real-time information about tissue morphology and molecular composition. He is the recipient of Starting Grants from the European Research Council and the EPSRC.



**Above:** ultrasound waves transmitted by an imaging probe used for tracking medical devices in the body.
**Below:** optical fibre with a nano-composite coating used for ultrasound transmission (scanning electron micrograph).

**GIFT-Surg focus:**

Imaging plays a central role in fetal surgery. Conventionally, our views of the placenta and the fetus from inside the uterus have been limited to white-light endoscopy. This modality provides a superficial view of tissue, without quantitative information about blood flow. One resulting limitation is that subsurface vessels, which can be of significant interest in procedures such as twin-to-twin transfusion syndrome (TTTS), are largely invisible. During fetal surgery, our views of the uterine environment from outside the body have been limited to ultrasound imaging, which has insufficient spatial resolution for many clinical contexts, and it does not directly provide information about the molecular composition of tissue.

Miniature photoacoustic and ultrasound imaging probes that can be inserted into the uterine environment could dramatically enhance our ability to visualise the placenta and fetus. They will provide depth-resolved images, so that subsurface structures such as blood vessels can be directly visualised. Photoacoustic imaging probes will involve the delivery of pulsed light to tissue to generate ultrasound waves, and the use of optical interferometry for reception. Ultrasound images will also be obtained with optical methods, which will include engineered nano-composite materials that transmit ultrasound when illuminated by pulsed light. These imaging probes will provide views of the placenta and fetus that are significantly higher in spatial resolution than those obtained from outside the body, and molecular specificity to provide contrast for blood oxygenation.

Visualisation of medical devices within the body is an important challenge in interventional procedures. Medical devices often stray from the ultrasound imaging plane, and the resulting uncertainties about their locations can increase the risk of complications and decrease procedural efficiency. Ultrasonic device tracking is a method for localising medical devices within the body that will be developed for fetal interventions. This method involves receiving ultrasound pulses from an external imaging probe using fibre optic ultrasound receivers, and processing the received pulses in a manner analogous to GPS tracking. With the information provided by ultrasonic device tracking, high-resolution photoacoustic and ultrasound images acquired from inside the uterus will be aligned in real-time to the large-scale ultrasound images acquired from outside the patient.

# Prof David Hawkes

UCL Professor of Medical Imaging Science

Professor David Hawkes is currently the Director of the Centre for Medical Image Computing, previously having been Director of the EPSRC and MRC funded Interdisciplinary Research Collaboration on Medical Images and Signals (MIAS-IRC), an £8M six year programme, from 2003 to 2007 and Chairman of the Division of Imaging Sciences at KCL (2002-2004). He spent 10 years working as a clinical scientist within the NHS before returning to academia. He is co-Founder of IXICO Ltd. (www.ixico.com), a university spin-out that provides imaging solutions to the pharmaceutical industry. His current research interests encompass image matching, data fusion, visualisation, shape representation, surface geometry and modelling tissue deformation promoting medical imaging as an accurate measurement tool and image guided interventions.

**GIFT-Surg focus:**

Professor Hawkes's role in the project will be to provide overall advice in image guidance technologies and clinical translation as well as specific expertise in the incorporation of active models and tissue sensing into image guidance systems.

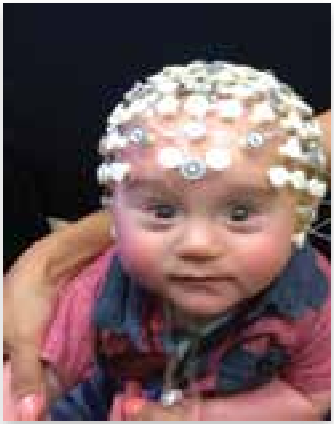
# Prof Neil Marlow

UCL Professor of Neonatal Medicine

Neil Marlow is Professor of Neonatal Medicine at University College London and current Chair of the NHS England Neonatal Critical Care Clinical Reference Group. He took up this appointment following 11 years as Professor of Neonatal Medicine at Nottingham and 7 years as Senior Lecturer in Bristol. He is an Honorary Consultant in the University College Hospital Neonatal Service. His major academic interests have been in long-term outcomes following prematurity and he is the Director of the MRC-funded EPICure studies (www.epicure.ac.uk). He runs a series of local studies into brain and cognitive development following very preterm birth and is a co-investigator on a range of mainly UK based cohort and randomised studies. Neil has been President of the British Association for Perinatal Medicine, Director of the UCL Institute for Women's Health, President of the European Society for Paediatric Research and Chair of two European Academy of Paediatric Societies Meetings. He was elected a Fellow of the Academy of Medical Sciences and is an Honorary Life Friend of Bliss, the UK-based charity for premature babies.

**GIFT-Surg Focus:**

Neil's role in the project is mainly in defining the efficacy and acceptability of fetal surgery. We anticipate that early testing and adoption of several technical innovations into clinical practice will be achieved during the lifetime of the project, but as yet it is not possible to define which arm will reach this stage. When new innovations are developed it is important to develop clear methods to define outcome and to consider if the innovation brings benefits to the patient and the families that look after them. Using his expertise developed over many years in neonatal outcome studies, Neil will develop condition-specific functional outcomes for the fetus, the baby and the mother including qualititative long term outcomes, after the innovative fetal surgeries have been applied. He will work with the PPI group to consider which are the best outcomes to measure. He will also help to develop ways to economically model the added value of the novel technologies.



## Prof Donald Peebles

UCL Professor of Maternal and Fetal Medicine/UCLH Consultant

Prof Donald Peebles is a graduate of Cambridge University and then Guys and St Thomas' Medical School. His MD thesis, obtained at UCL, described the use of near infrared spectroscopy for assessing fetal brain oxygenation during labour. Much of his research since then has used MR and NIRS spectroscopy and imaging to investigate the effects of hypoxia and infection on the developing brain. He has been Head of the Research Department of Maternal Fetal Medicine at UCL since 2008. He has a number of research interests that focus on improving the outcomes for women and their babies following complicated pregnancies. Particular research areas include: 1) maternal innate immunity, infection, inflammation and preterm labour 2) the role of hypoxia and inflammation in causation of perinatal brain injury 3) fetal physiology (especially fetal responses to acute and chronic substrate deprivation) and 4) the development of novel molecular and cellular methods for treatment of fetal disease.

He is also a Consultant at UCLH with sub-specialty accreditation in Maternal Fetal medicine in 1990. He provides a range of diagnostic and therapeutic services on the Fetal Medicine unit with particular interests in the management of fetal growth restriction as well as the management of fetal rhesus disease. He is a faculty member of the Infection, inflammation and Immunity Theme of the NIHR UCLH Biomedical Research Centre.

**GIFT-Surg focus:**

To ensure that the major advances in fetal imaging and instrumentation that will come from this grant lead to improvements in outcome for fetuses with a range of congenital abnormalities. Particular clinical challenges include the difficulty of accessing fetal blood vessels and organs as early as twelve weeks gestation (when the fetus is only 5cms long), optimizing the therapy that will be delivered (eg cells, genes or surgical accessories such as balloons or patches), ensuring patient safety and engaging with stakeholders to address ethical concerns at an early stage in the development of new techniques. This will involve a staged process of experimentation using phantoms to model the anatomy of the early pregnancy gestation sac/fetus, suitable animal models and finally the first in human experiments/optimizing existing fetal surgery procedures. A particular focus will be the use of improved imaging and registration techniques to improve clinical training in commonly used fetal medicine diagnostic and therapeutic techniques to reduce the risk of miscarriage or early delivery.

# Prof Dominiek Reynaerts

KUL Professor of Mechanical Engineering

Prof Reynaerts is chairing the Dept. of Mechanical Engineering of KU Leuven since 2008. He is a member of the Nanotechnology Research Centre of KU Leuven. As department chair he is also member of the management board of the Science and Technology CoreLabs of KU Leuven, this is a centralised high-tech facility for advanced equipment. He is a member of IEEE and Euspen. During his PhD he was a visiting researcher at the Scuola Superiore di studi universitari e di perfezionamento S. Anna, Pisa, Italy.

He is a member on various scientific national and international review committees and management boards: Scientific Advisory Board Delft Center for Microsystems & Mechatronics (2006-2008) and Mid-term review committee MicroNed programme, NL (2007), IOF (Industrial Research Fund) KU Leuven (2006-08), MultiMaterial Micro Manufacturing FP6 NoE (Executive board 2004-06), Member board FMTC (Flanders Mechatronics) (2013-now), and Panel member of Scientific Committee “Energy, Electrical Engineering, Electronics and Mechanics” of the Research Foundation – Flanders (2010-2016). He was a participant in 12 EU projects, 3 of which were as a coordinator. Out of his research group 3 spin-offs were already created, one of which is in surgical robotics, and he is mentioned as inventor on 5 patents. A major technological achievement has been the speed record of 1.2 million rpm on air bearings established by his research group.

**GIFT-Surg Focus:**

Prof Reynaerts is an expert in manufacturing and machine design with focus on precision engineering and micromechanical systems, with major applications in surgical instruments, precision machines and smart actuators.

# Prof Alexander Seifalian

UCL Professor of Nanotechnology and Regenerative Medicine

Prof Seifalian is a Professor of Nanotechnology and Regenerative Medicine, and director of UCL Centre for Nanotechnology & Regenerative Medicine at University College London (UCL-CNRM).

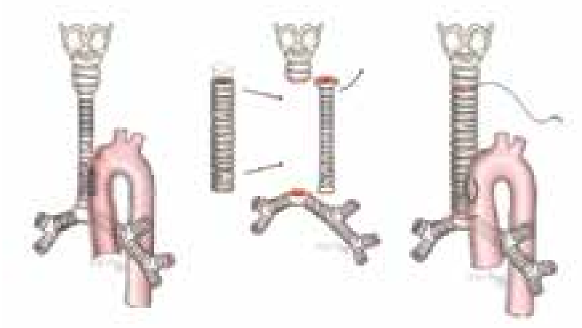
He completed his education at University of London and University College London Medical School. He is a Fellow of the Institute of Nanotechnology (FIoN) and Fellow of Society of Biology (FSB), and has published over 400 peer-reviewed research papers, 31 book chapter contributions and 10 families of UK and International patents.

During his career he has led and managed many large projects with multidisciplinary teams with very successful outcomes in terms of commercialisation and translation to patients including: 1) The development and commercialisation of a bypass graft for vascular access for haemodialysis; 2) The development of bioreactors with fluid dynamic systems; 3) Derived non-invasive techniques to monitor shear stress in vivo as well as on cells in a physiological flow circuit using RF ultrasound signalling; 4) Developed laser activated vascular sealants that have been commercialised for vascular, liver and brain surgery, and 5) As part of an EU grant, he worked on the development of a miniature implantable portal blood pump. His role involved designing the pump for biocompatibility and in vivo evaluations.

**GIFT-Surg Focus:**

Alex's current projects have led to the development of many human organs using nanotechnology based materials and stem cells technology. The organs already in human include the world's first synthetic trachea, bypass graft, tear duct, nasal reconstruction and filler.

He has also developed a family of nanomaterials and nanocomposite polymers for a range of biomedical applications. Alex will be working on the regenerative medicine workpackage and applying his expertise into developing patches and other therapies that can be used inside the womb.

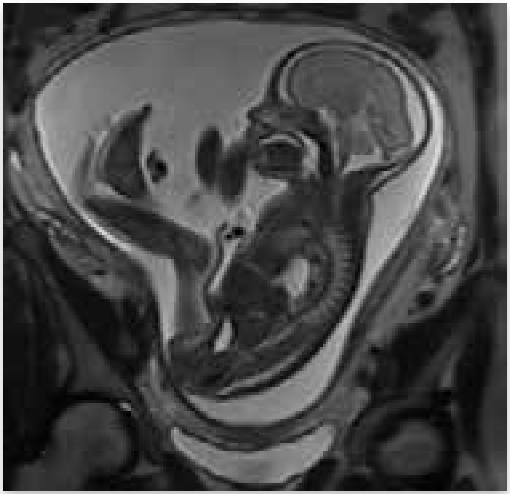


**Above:** Diagram illustrating repair of a damaged oesophagus

# Dr Tom Vercauteren

UCL Senior Lecturer in Interventional Imaging

Dr Tom Vercauteren is a Senior Lecturer within the Translational Imaging Group at UCL, which he joined in May 2014. He is a graduate from Columbia University and Ecole Polytechnique and obtained his PhD from Inria Sophia Antipolis. His main research focus is on the development of innovative interventional imaging systems and their translation to the clinic. One key driving force of his work is the exploitation of image computing and the knowledge of the physics of acquisition to move beyond the initial limitations of the medical imaging devices that are developed or used in the course of his research. During his previous industrial experience, he led the research and development to design, develop and integrate a complete image computing pipeline for a clinical optical biopsy device with CE mark and FDA clearance for gastrointestinal applications currently used in hundreds of hospitals worldwide.



**Above:** MRI scan of fetus

**GIFT-Surg Focus:**

One ambition within GIFT-Surg is to develop an integrated surgical platform for intrauterine fetal surgery. As highlighted in this booklet, this requires a combination of multidisciplinary expertise to lead the development of the main building blocks for this platform. Within this project, work will focus on designing new surgical manipulators, new intra-operative imaging devices, new data fusion tools and new surgical planning and guidance solutions.

Tom Vercauteren's main role in GIFT-Surg is to drive the integration of the different software and hardware components into interventional systems that will help the physicians in delivering better patient outcomes.

A complete interventional system needs to link many different elements starting from a surgical planning phase where a pre-operative, fetus-specific model of the anatomy and pathology is constructed using pre-operative data such as external 3D ultrasonography or MRI if the intervention requires detailed information about the surrounding maternal anatomy. The pre-operative model then embeds biomechanical information to be able to compute and predict the deformations that may occur during the surgery. Intra-operative imaging, including the novel modalities developed in the course of the project, can then be used both to provide information about key physiological parameters and also to deform the model and align it with the anatomy, accounting for motion and deformation of the foetus as well as the maternal anatomy. This allows providing information feedback to the surgical manipulators and can also be used to map pre-operative data with the current context of the procedure thereby enhancing the interventional information available to the physician.

Focusing on system integration from the onset of the project plays a key role in ensuring that developments can be safely translated to the clinic.

# Prof Kypros Nicolaides

Professor of Fetal Medicine

Kypros Nicolaides studied medicine at King's College School of Medicine and Dentistry in London and soon after graduation joined the Department of Obstetrics and Gynaecology in 1980, doing research with Professor Stuart Campbell and Professor Charles Rodeck as his first assistant, working mainly on fetoscopic techniques and procedures. He was well known for his manual dexterity at procedures and the Rodeck-Nicolaides team soon produced some very important papers on the use of fetoscopy in the management of a wide range of conditions such Rhesus iso-immunization, fetal hydrops and intrauterine growth restriction, and procedures such as blood and tissue sampling in the diagnosis of single gene defects.

After the departure of Professor Rodeck, Nicolaides became director of the Harris Birthright Research Centre for Fetal Medicine, the first fetal medicine unit in the United Kingdom.

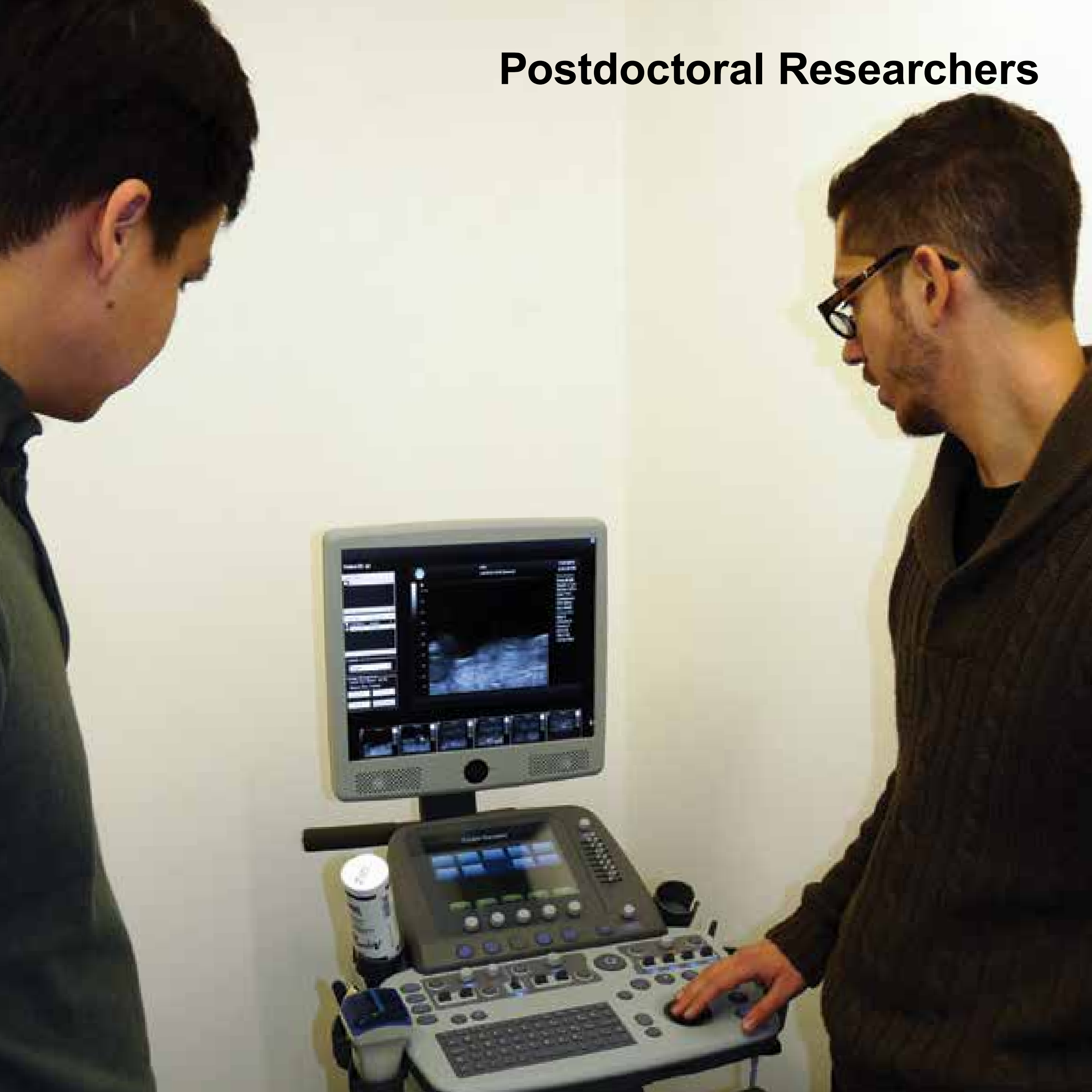
He has contributed to over one thousand journal articles and more than thirty books and monographs.

Concluding a major part of his work over the years regarding the 11-13 weeks scan assessment (including measurement of nuchal translucency) he has proposed a new model of pregnancy care "Turning the Pyramid of prenatal Care". This model shows that it is now possible to assess the risk for most of the relevant complications affecting mother and unborn child if combined screening tests are carried out in a specialist outpatient clinic following protocols published by The Fetal Medicine Foundation. Assessing the risk for those pregnancy complications at such an early time in pregnancy this might doctors not just give the chance to reassure patients but also to prevent some of these complications (such as Pre-Eclampsia or Premature Birth). Those complications are major contributors to maternal and neonatal morbidity and mortality.

**GIFT-Surg Focus:**

Kypros will provide expertise on the use of fetoscopic techniques and procedures as well as insight into surgical processes.

# Postdoctoral Researchers



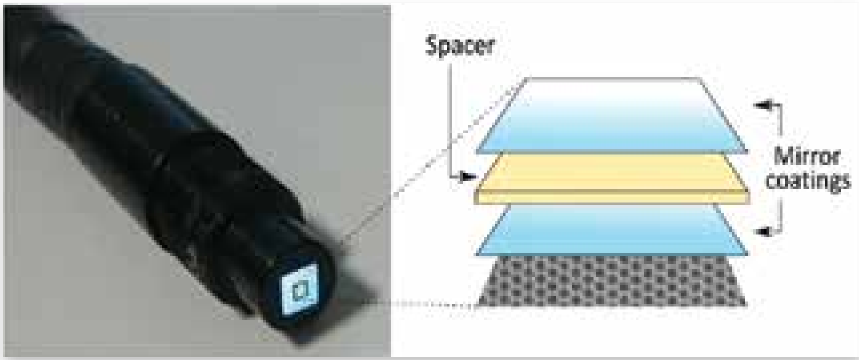
# Dr Rehman Ansari

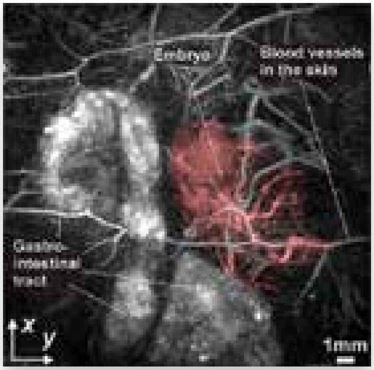
UCL Postdoctoral Research Associate

Rehman Ansari is a post-doctoral research associate in the Photoacoustic Imaging Group in the Department of Medical Physics and Biomedical Engineering, University College London. He received a Master's degree in Biomedical Engineering from New York University School of Engineering, New York. He obtained his PhD from the University of Luebeck, Germany, where his research focus was on development of phase sensitive optical coherence microscopy systems, and its applications in medicine and life sciences.

**GIFT-Surg Focus:**

Rehman is working on the development of miniaturized photoacoustic endoscopy probes for guiding fetal interventional procedures. Photoacoustic tomography is particularly well suited for visualising the structure and function of the vasculature, as it provides selective absorption contrast. The goal is to develop all-optical, forward and side-viewing miniaturized 3D imaging probes using coherent fibre bundles and Fabry-Pérot (FP) ultrasound sensors. The fibre bundle comprises several thousand elements, which have micron-scale diameters, and illuminates the FP sensor which is deposited at the distal end. In this way, the FP sensor acts as a 2D array of ultrasound detectors at the tip of the bundle. This new approach to photoacoustic endoscopy offers several advantages over previous distal-end scanning probes. These include a high degree of miniaturisation, no moving parts at the distal end and the potential for relatively simple and inexpensive fabrication.




**Left:** All-optical photoacoustic endoscopy probe with a Fabry-Pérot sensor on tip of the fibre bundle.

**Right:** Representative photoacoustic image of a pregnant mouse abdomen with an embryo shown in red (acquired using a non endoscopic FP scanner), Laufer J, Norris F, Cleary J, Zhang E, Treeby B, Cox B, Johnson P, Scambler P, Lythgoe M, Beard P (2012) In vivo photoacoustic imaging of mouse embryos, Journal of Biomedical Optics 17(6), 061220.

# Dr Francois Chadebecq

## UCL Postdoctoral Research Associate

François Chadebecq has recently completed his PhD in Computer Vision at Université d'Auvergne under Dr Christophe Tilmant and Prof Adrien Bartoli with a dual affiliation to the ComSee group at Institut Pascal and ALCoV. He received his MSc degree in Computer Science with honors at Université Blaise Pascal in 2010. His PhD research aims at developing a passive computer vision method to measure the size of tumours in colonoscopy. With the help of his supervisors, he proposed an innovative method adapted to the prime lens optical systems of colonoscopes, to extract the sharp/blur breakpoint (named the Infocus-Breakpoint) in a video stream obtained by moving the colonoscope toward a neoplasia (Chadebecq et al., MIA 2015). His research interests include 3D reconstruction and its applications in colonoscopy.

### GIFT-Surg focus:

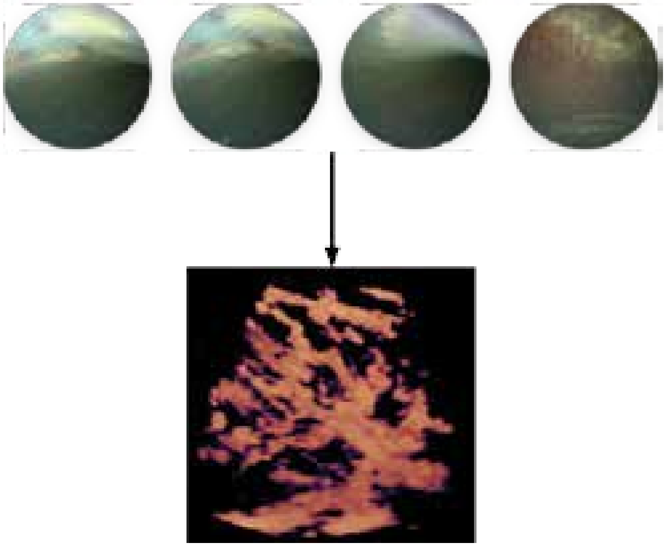
François Chadebecq joins the GIFT-Surg project in January 2015 as a post-doctoral research associate with the aim to develop 3D reconstruction techniques to advance real-time information processing of images acquired in utero using a fetoscope.

**Above:** Screen shot from endoscopic video footage of the hand of an unborn baby in the womb.

# Dr Pankaj Daga

UCL Postdoctoral Research Associate

Pankaj obtained his Bachelor of Science degree in Computer Science from University of Maryland University College in 2000. He worked on diverse projects as a software engineer until 2009 before obtaining his MSc in Medical Image Computing (2009), followed by a PhD in image guided surgery at UCL (2014). Pankaj is currently a senior postdoctoral research associate working on novel image analysis methods for image-guided fetal surgery. More specifically, he works on real time mosaicking of fetoscope images and motion compensated fetal MRI reconstruction.



**Above:** A 3D model of the placenta can be generated from a series of 2D limited field of view fetoscopic images.

**GIFT-Surg focus:**

Twin-to-twin transfusion syndrome (TTTS) is a complication that affects 10-15% of identical twins who share a placenta. The disease results from an imbalance in the blood circulation between the twins due to the presence of anastomoses in the shared placenta. Without intervention, the condition can be fatal for both twins in severe cases. Laser coagulation of the connecting vessels on the placenta between the twin fetuses can be a curative procedure in advanced stages of TTTS. Under fetoscopic video guidance, the surgeon uses a laser fiber to coagulate the blood vessels that connect the two fetuses. This involves visually inspecting the entire placenta to identify the crossing blood vessels that contribute to placental anastomoses before coagulating them.

A key limitation of fetoscopic image guidance is the limited field of view. Pankaj is developing novel image analysis techniques that can generate a full 3D model of the placenta from a series of limited field of view 2D fetoscopic images. This will enable the surgeon to visualize the complete placenta and the vascular structures of interest allowing more efficient surgical planning and navigation, whilst minimizing the risk of missing anastomoses.

This work is done in collaboration with Marcel Tella Amo, Tom Vercauteran and Prof Jan Deprest (UZ Leuven, Belgium).

# Dr Tom Doel

UCL Postdoctoral Research Associate

Tom is a postdoctoral researcher in medical image analysis and an experienced clinical software developer. At Barco Medical Imaging Systems he developed clinical visualisation and analysis software used by radiologists worldwide. His PhD at the University of Oxford involved developing novel disease measures using image analysis and computational modelling, as part of a clinical trial into hyperpolarised gas MRI. Tom continued this work at Oxford as a postdoctoral research associate, and also worked on the Synergy-COPD project as part of the Virtual Physiological Human collaboration. He has an MSc in applied mathematics from the University of Bath and an MPhys in mathematical physics from the University of Edinburgh.


**Above:** Software and hardware platform design and integration in WP9: Clinical-grade applications for pre-operative surgical planning and image-guided surgery, using state-of-the-art software algorithms to combine pre-operative images with real-time processing of live surgical data.

**GIFT-Surg Focus:**

Along with Dzhoshkun Shakir, Tom is building the software platform that will bring the GIFT-Surg research into practical use within the clinical environment, integrating the novel hardware and software developed by the GIFT-Surg team. Their aim is to provide a state-of-the-art clinical application suite for pre-operative surgical planning and image-guided intervention for aiding surgeons in fetal surgery. Furthermore their data-sharing platform will facilitate secure information exchange between collaborating institutions.

Their work includes the following components:
Clinical-grade applications for pre-operative surgical planning and image-guided surgery, using state-of-the-art software algorithms to combine pre-operative images with real-time processing of live surgical data.

Robust integration of novel hardware, calibration procedures, steering interfaces, real-time control and hardware device communication mechanisms.

GIFT-Surg SDK – a flexible, modular, extensible software platform to facilitate the rapid development of image analysis algorithms, built on the imaging expertise of CMIC and tailored to the needs of researchers.

GIFT-Cloud – a secure collaboration platform for sharing data between institutions, offering seamless data integration between data providers and the software platform, while protecting sensitive patient information via industry-standard anonymisation and encryption.

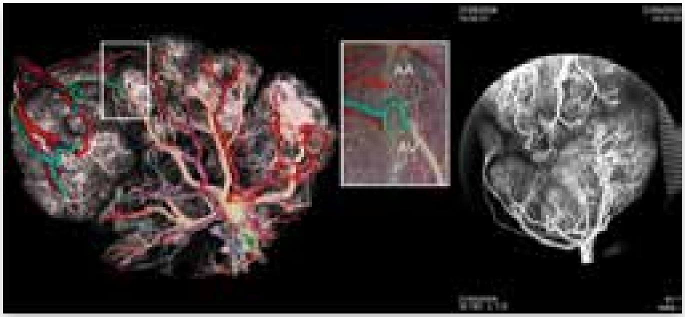
# Dr Alexander Engels

KUL Clinical Research Associate

Alexander Engels obtained his Medical Degree in 2012 at the University of LMU Munich, Germany. In 2014 he started a PhD in the Department of Development and Regeneration at the KU Leuven. His research and clinical work focusses on fetoscopic surgery and the prevention of preterm premature rupture of fetal membranes.

**GIFT-Surg Focus:**

Alexander joined the project recently and is a clinical research fellow of Prof Jan Deprest. He is involved in clinical applications and investigations in surgical models.

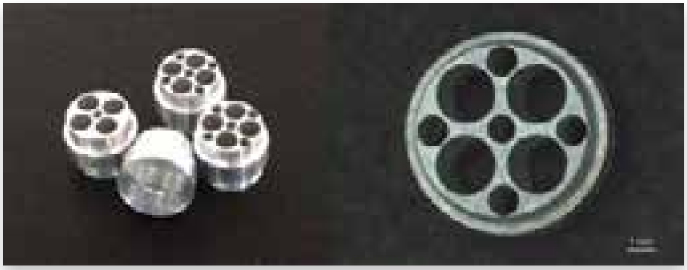


**Above:** Images of the placenta which have had a dye applied to better highlight the veins and arteries of monochronionic twins (twins whom share the same placenta and circulatory system) to identify anastomosis for research and training purposes.

# Mr Caspar Gruijthuijsen

KUL Research Associate

In 2011 Caspar completed his BSc in Mechanical and Electrical Engineering and in 2013 he obtained his MSc in Mechanical Engineering at KU Leuven, Belgium. Throughout his studies attention was drawn to the challenging research field of medical technology. As such Caspar's master thesis project dealt with robotic control of catheters in the cardiovascular system. In particular he is interested in the recent evolutions of surgical instruments. Through novel designs, integrated sensing and precise control, these instruments are turning into intelligent devices capable of accomplishing very precise and delicate interactions with the human body. Therefore immediately after graduating he started a PhD on surgical robotics and instrument design at the Robot Assisted Surgery (RAS) group of the Mechanical Engineering Department at KU Leuven.



**Above:** View upon components of the dual-segment fluidic-actuated instrument produced at KUL through precision manufacturing techniques.

**GIFT-Surg focus:**

Within the GIFT-Surg project important developments with respect to surgical instrumentation for fetal surgery will be realized. This mechanical aspect of the project is in the hands of the RAS group at KU Leuven. Novel single-arm and multi-arm instruments for augmented dexterity in fetal interventions will be developed. To support these instruments a self-aware synergetic stabilizer and adequate control strategies will also be designed. Although personal research interests go to all of these topics and there is very high collaboration between all researchers within the RAS-group working on GIFT-Surg, Caspar's research will focus on the design of the stabilizer for fetoscopic instrumentation.

Fetal interventions are very delicate procedures, requiring full concentration from the surgeon to perform precise manipulation on the unborn child. To alleviate the critical tasks for the surgeon Casper will design a mechanical device that is capable of stabilizing the fetoscopic instruments. This stabilizer will be flexible in use, in such a way that it can be deployed regardless of the position of the fetoscope entry point and without limiting the workspace of the surgeon. The stabilizer won't attempt to replace the surgeon, but rather aim at reaching an optimal synergy between human ability and advanced technology. The load will be shared as such that the surgeon's intelligence and skill will be complemented with dexterity enhancement from the stabilizing device.

# Dr Luc Joyeux

KUL Clinical Research Associate

Luc Joyeux is a French M.D., board certified in general pediatric surgery and specialized in maternal-fetal medicine, minimally invasive and robotic surgery. He obtained an American M.D. degree in 2006 from the United States ECFMG (Educational Commission for Foreign Medical Graduates) and a Master's degree in surgical science from the University of Paris XI-XII in 2009. He worked one year (2008-2009) as a research fellow on fetal gene therapy in the center for fetal research of professors N.S. Adzick and A. Flake at the Children's Hospital of Philadelphia. He is starting a Ph.D. in the Academic Department of Development and Regeneration, Organ System Cluster, of professor Jan Deprest at the University Hospitals Leuven.

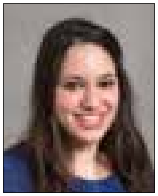
**GIFT-Surg Focus:**

Luc's research, part of GIFT-Surg, is dedicated to reduce the invasiveness of fetal spina bifida aperta (SBA) surgical repair with novel instrumentation. Open maternal-fetal surgery (OMFS) for SBA is a feasible, secure and more efficient therapeutic option compared to postnatal surgery. However OMFS is an invasive technique increasing the risks of preterm rupture of membrane, preterm labor, prematurity for the fetus and the risks of the double hysterotomy for the mother. The protocol will explore the feasibility for fetoscopic repair by single access, as well as an early gestational repair, using purpose designed techniques and alternative repair methods.

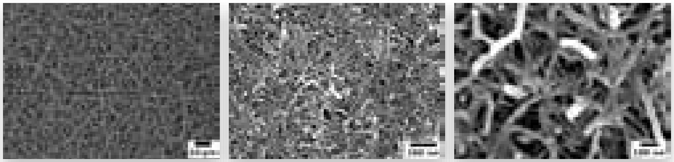
**Above:** A fetoscopy. Denise Pedreira, CC-BY-SA 3.0

# Dr Sacha Noimark

UCL Postdoctoral Research Associate



Sacha obtained her undergraduate MSci degree in Chemistry with Mathematics (2010) at University College London. She then joined the UCL M3S Centre for Doctoral Training and received an MRes in Molecular Modelling and Material Science (2011) as part of the EngD programme. Her EngD research was focused on the synthesis of light-activated antimicrobial materials for hospital touch-surface and medical device applications. She is currently a post-doctoral research associate at the UCL Department of Chemistry and the UCL Department of Medical Physics and Biomedical Engineering, working on the development of nanostructure-polymer composite materials for laser-generated ultrasound.



**Above:** Scanning electron micrographs of materials currently being considered for laser generated ultrasound, including electrospun fibres with integrated carbon nanotubes (left), and functionalised multi-walled carbon nanotubes dip-coated on a glass substrate (centre and right).

**GIFT-Surg focus:**

Ultrasound imaging is an invaluable tool in fetal medicine. Visualisation of the placenta and the fetus has conventionally been performed with ultrasound imaging probes positioned at the surface of the body. One of the central objectives of the GIFT-Surg project is to develop probes that can provide visualisation from within the uterus. For fetal interventions, miniaturisation of intra-uterine ultrasound imaging probes is of great importance. However, achieving miniaturisation and high image quality using traditional piezoelectric transducers or capacitive micro-machined ultrasonic transducers can be challenging.

Recent research has shown rapid progress in the development of optical ultrasound transducers. These transducers generate ultrasound through exploitation of the photoacoustic effect and this approach can circumvent many of the limitations posed by electrical transducers. Sacha's research is focused on the development of nanostructure-polymer composite materials for laser-generated ultrasound. Optical ultrasound transducers will be developed through the deposition of carbon nanostructure-polymer composite coatings onto optical fibres. To optimise these probes for ultrasound generation, a range of absorbing species will be considered, including carbon nanotubes (multi-walled and single-walled) and graphene, utilising deposition techniques such as dip-coating, electrospinning and inkjet printing. Further work will entail the development of nanostructure-polymer composite coatings that demonstrate high absorption at particular wavelengths and transparency at other wavelengths, such that these probes can be used for both ultrasound generation and other imaging techniques or therapies.

# Dr Rosalind Pratt

UCL Clinical Training Fellow (STr)

Dr Rosalind Pratt is currently working in North East London as trainee in clinical obstetrics and gynaecology with the Barking, Havering and Redbridge University Hospitals NHS Trust.

From January 2015 Rosalind will be taking time out of her clinical training to joint the GIFT-Surg team, where she will take on the role of Clinical Academic Research Fellow.

**GIFT-Surg Focus:**

Innovations developed in the project will open the way for new treatments that are currently not possible due to the difficult constraints of operating in the intrauterine environment. Rosalind will work with the team to develop and run a prospective study collecting detailed information from pregnancies that undergo current fetal imaging by MRI and ultrasound, and fetal surgery. She will also develop algorithms or methods that will improve visualisation and treatment of the fetus undergoing fetoscopy and ultrasound/MR imaging and develop standard operating procedures for innovations in clinical practice. She will coordinate ethical approval for the novel imaging platforms in the clinic and develop a framework to evaluate patient acceptability and efficacy after innovative surgery.

Rosalind will also support the development of a training platform that will enable fetal surgeons to gain the necessary skills in the instruments before operating on pregnant mothers. She will review the bioethics of innovation in fetal surgery lead by Professor Richard Ashcroft, a bioethicist from Queen Mary University of London, and set up and run a patient public engagement group to consider all aspects of the project innovations as they emerge during the research.

# Dr Benoit Rosa

KUL Postdoctoral Research Associate

Benoit obtained his Engineering Degree from Ecole Centrale Paris in 2009, and his Ph.D. from Pierre & Marie Curie University (Paris) in 2013. During his PhD, he worked on the control of the micron-scale movements of a confocal endomicroscopy probe for the purpose of making optical biopsies, using a combination of mechanical tools (stabilization, handheld purposely-designed instrument) and imaging (visual servo control of the probe movements). Since July 2013, he is a postdoctoral fellow at KU Leuven, within the Robot-Assisted Surgery group of the Mechanical Engineering Department. His research interests lie in the design and control of surgical robots and devices for helping the surgical gesture, as well as in intuitive ways of controlling flexible and bendable surgical instruments.

**GIFT-Surg focus:**

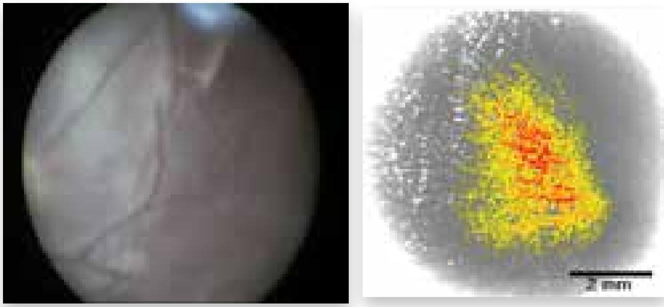
In the GIFT-Surg project, the role of the KU Leuven team lies in the design and control of surgical instrumentation, namely a stabilizer for helping the surgeon to make precise and stable gestures, a single-arm bendable instrument to reach target areas of the fetus with accuracy, and a multi-arm instrument for complex interventions. Though Benoit has interests in all those developments, it lies particularly in the two latter, combining micro-actuation with bendable flexible devices. During Benoit's Masters and PhD, he designed and made three different prototypes of small-scale medical instruments for precisely controlling intra-operative movements of surgical tools (laser) and imaging devices (camera, confocal endomicroscope). This expertise will be applied to the design of the surgical instrumentation that is being developed at KU Leuven for the GIFT-Surg project. His experience in designing surgical devices and experiments, going from lab bench-testing to in vivo pre-clinical experiments, will also be an important asset at this point.

**Above:** Concept design of single-arm bendable instrument. KU Leuven.

# Dr Gustavo Santos

UCL Postdoctoral Research Associate

Gustavo joined the Translational Imaging Group as a postdoctoral research associate in August 2014 to develop new imaging tools for image-guided fetal surgery. Prior to this, he was a research associate at the Electrical Impedance Tomography group also at UCL (2011-2014). For his PhD, he did research in Computational Neuroscience at RIKEN Brain Science Institute and the University of Tokyo in Japan (2006-2011). He obtained his undergraduate (2002) and M.Eng. (2006) degrees in Electrical Engineering and Computer Science from MIT.




**Above:** example laser speckle contrast image showing the blood perfusion in the skin of the hand.

## GIFT-Surg Focus:

The aim of Gustavo's research is to integrate new intraoperative imaging modalities for minimally-invasive fetal surgery, and to develop novel methods for extracting and displaying critical physiological parameters for guiding surgeries. Currently, surgeons are limited to video imaging through the fetoscope and external ultrasound imaging, which provide very little information from inside the uterus. Enhancing the fetoscope with new imaging modalities - such as fibre-optic ultrasound and photo-acoustic imaging - will greatly extend our ability to obtain quantitative physiological information about the fetuses and placentas.

His initial focus is to enable the surgeon to visualise blood perfusion in the placenta, particularly in Twin-to-Twin Transfusion Syndrome (TTTS). For treatment of TTTS, surgeons need to accurately characterise the placental vasculature and photocoagulate vessels to stymie the flow of blood between twins. However, there is currently no way to assess the photocoagulation process during the operation, or to identify anastomoses deeper in the placental tissue where blood exchange may also be occurring between the twins. He is currently working to develop a fetoscopic implementation of laser speckle contrast imaging, which will be used to estimate blood flow in superficial vessels in the placenta (see figure). Studies are being performed in phantoms and ex vivo human placentas, and the methods will subsequently be tested in an animal model. In future studies, he will use fibre-optic photoacoustic and optical ultrasound imaging to identify anastomoses deep in the placenta.

# Dr Dzoshkun Shakir

UCL Postdoctoral Research Associate

Dzoshkun has a BSc in Computer Engineering (2006) from Bilkent University, Turkey and an MSc in Computational Science and Engineering (2009) from Technical University Munich, Germany. In 2014 he obtained his PhD with a dissertation entitled “Intra-operative Nuclear Imaging Based on Positron-emitting Radiotracers” under supervision by Prof Nassir Navab (Computer Science) and Prof Sibylle Ziegler (Medical Physics) at Technical University Munich, Germany. His PhD work focused on the development of two novel intra-operative imaging modalities for guidance in cancer surgery. Being highly interested in computer-aided interventions and image-guided surgery, he joined the Translational Imaging Group at UCL as a post-doctoral research associate shortly after completing his PhD.

**GIFT-Surg focus:**

Along with Tom Doel, he is building the software platform that will bring the GIFT-Surg research into practical use within the clinical environment, integrating the novel hardware and software developed by the GIFT-Surg team. Their aim is to provide a state-of-the-art clinical application suite for pre-operative surgical planning and image-guided intervention for aiding surgeons in fetal surgery. Furthermore their data-sharing platform will facilitate secure information exchange between collaborating institutions.

Their work includes the following components:

- Clinical-grade applications for pre-operative surgical planning and image-guided surgery, using state-of-the-art software algorithms to combine pre-operative images with real-time processing of live surgical data.

- Robust integration of novel hardware, calibration procedures, steering interfaces, real-time control and hardware device communication mechanisms.

- GIFT-Surg SDK – a flexible, modular, extensible software platform to facilitate the rapid development of image analysis algorithms, built on the imaging expertise of CMIC and tailored to the needs of researchers.

- GIFT-Cloud – a secure collaboration platform for sharing data between institutions, offering seamless data integration between data providers and the software platform, while protecting sensitive patient information via industry-standard anonymisation and encryption.

**Left:** Software and hardware platform design and integration in WP9: GIFT-Cloud will provide a secure collaboration platform for sharing data between institutions, offering seamless data integration between data providers and the software platform, while protecting sensitive patient information via industry-standard anonymisation and encryption.

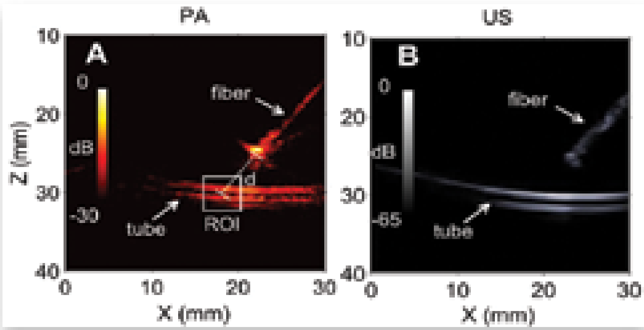
# Dr Wenfeng Xia

UCL Postdoctoral Research Associate

Wenfeng received a BSc in Electrical Engineering from Shanghai Jiao-Tong University, in Shanghai, China, in 2005 and an MSc in Medical Physics from University of Heidelberg, in Heidelberg, Germany, in 2007. His graduation project was performed in the Mannheim Biomedical Engineering Laboratories, in Mannheim Germany, focusing on the feasibility study of dental caries removal by picosecond and femtosecond laser ablation. After that, he was an Assistant Researcher in the Institute of Biomedical Optics, Luebeck, Germany, in a project on monitoring and automate control of the therapeutic temperature during retinal photocoagulation utilizing a photoacoustic temperature probe. From 2009 to 2013, he was a PhD student in the Biomedical Photonics Imaging group, University of Twente, Enschede, the Netherlands, developing a 3D photoacoustic mammography laboratory prototype system based on a computed tomography configuration. After receiving a PhD in 2013, he spent one year as a Postdoctoral Researcher to convert the laboratory prototype to a clinical version. He is currently a Postdoctoral Research Associate in the Photoacoustic Imaging Group at UCL, working on interventional photoacoustic imaging and ultrasound devices tracking.

**GIFT-Surg Focus:**

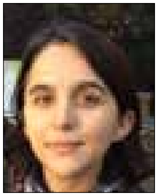
Precise image guidance is of great importance for minimally invasive fetal surgeries such as those performed to treat twin-to-twin transfusion syndrome (TTTS). Currently, therapeutic interventions for TTTS involve the identification of anastomosing vessels on the placenta using a fetoscope, followed by photocoagulation using a continous laser. Inadequate or missing coagulation of the placental anastamoses increases the failure of the procedure. One of the limitations of conventional fetoscopes is that they can provide insufficient sensitivity for vasculature that lies beneath the surface of the placenta due to strong light scattering in biological tissues. Photoacoustic (PA) imaging is a hybrid imaging modality that combines light absorption and ultrasound (US) propagation. It can provide both optical absorption contrast and spectroscopic specificity and subsurface visualisation of vasculature. It has strong potential to image placental and fetal vasculature with high sensitivity and specificity. In parallel with their developments of photoacoustic imaging, they are developing device tracking systems to precisely track needles that are inserted with ultrasound imaging. With their ultrasonic needle tracking approach, an optical hydrophone is attached to the device to receive transmissions from the transducer array. These received transmissions can be processed to obtain a clear image of the needle tip.



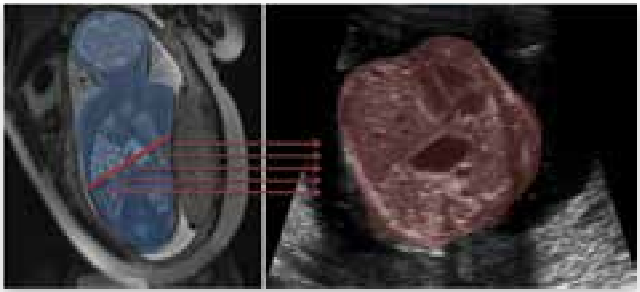

**Above:** photoacoustic (left) and ultrasound (right) images of a vessel phantom, with excitation light provided by a fibre adjacent to the vessel (tube).

# Dr Maria Zuluaga

UCL Postdoctoral Research Associate



In 2011, Maria obtained her PhD degree from Université Claude Bernard Lyon where she investigated automatic methods for the diagnosis of coronary artery disease. After a year as a postdoctoral fellow at the European Synchrotron Radiation Facility (Grenoble, France), she joined CMIC, in March 2012, as a Research Associate to work on cardiovascular image analysis and computer-aided diagnosis (CAD) of cardiovascular pathologies. Since August 2014, she has been a part of the GIFT-Surg project as a postdoctoral research associate.



**Above:** Anatomical information extracted from MR (blue) is propagated into US to guide segmentation.

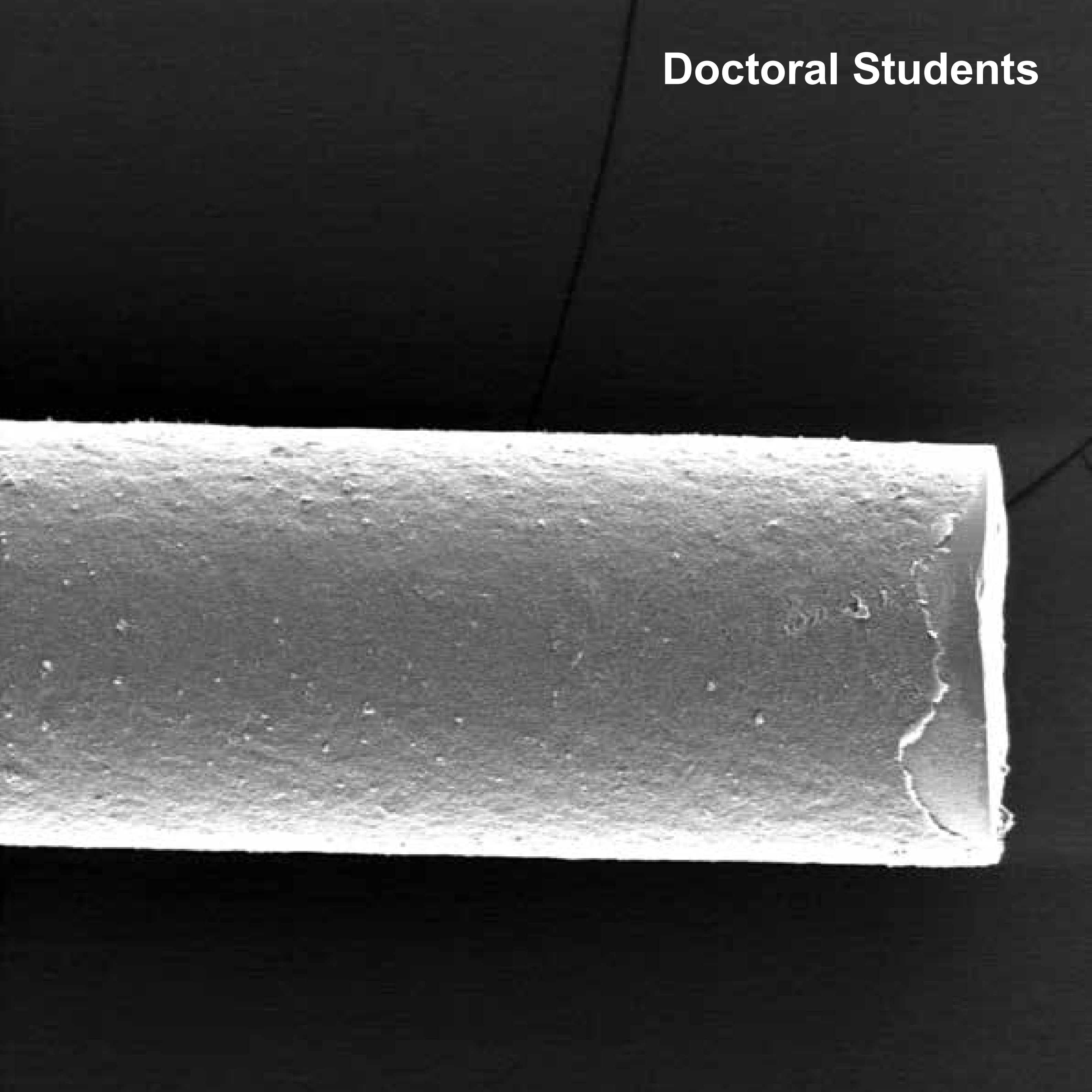
**GIFT-Surg focus:**

Pre-surgical planning plays a key role in assuring the success of fetal surgery. It comprises the extraction of the fetal anatomy and the localisation of the placenta to assist port placement. An optimal port placement guarantees the improved access of probes and instruments into the placenta. In this project, Maria will be involved in the development of novel image segmentation and modeling techniques to advance anatomy and pathology identification that are required for subsequent risk analysis, surgical planning, outcome prediction, and guidance during the intervention.

In the presence of complex pathologies, the extraction of both the fetal anatomy and the placenta can be a challenging task. To overcome these difficulties, we will be using different image modalities that can complement each other in the segmentation task. As ultrasound can be significantly affected by noise, Maria's main focus will be on the use of a priori anatomical information from an image modality with high spatial resolution (such as MRI) to guide and improve the spatio-temporal segmentation in ultrasound sequences, which is the standard modality in fetal imaging.

This work is done in collaboration with Guotai Wang, Ioannis Korouklides, Tom Vercauteren and scientists and clinicians from KU Leuven.

# Doctoral Students



# Mr George Dwyer

UCL Doctoral Student (PhD)

George started off at Swansea University in Wales, studying for a BEng in Medical Engineering. During which, he discovered his interest in design of surgical instruments and specifically the improvements that could be made with the integration of robotics. Graduating from Swansea in 2013, he started a MRes in Medical Robotics and Image Guided Intervention at Imperial College London, where he worked on the design of a scanning mechanism for intraoperative fusion of endomicroscopy and ultrasound. He is now a doctoral student in the EPSRC Centre for Doctoral Training in Medical Imaging within CMIC and is specifically part of the surgical robot vision group.

**GIFT-Surg Focus:**

The complexity of fetal surgery demands high quality visualisation of the surgical environment both in terms of resolution and field of view. George's research focus is on designing and improving fetoscopic instrumentation carrying optical or acoustic channels in order to enable flexible scanning and enhance the field of view of the intraoperative imaging. Different robotic scanning mechanisms can be used for this purpose depending on the size of the probe, the capabilities of the imaging modality and the anatomical targets under investigation.

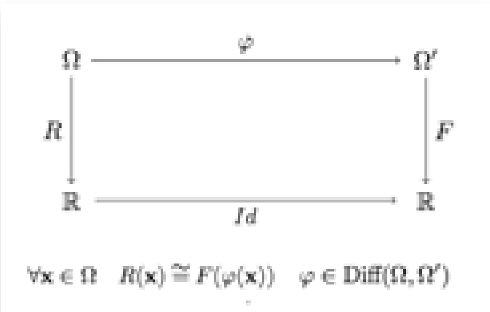
For imaging probes with a diameter in the millimeter scale, for example for photo-acoustic tomography, which uses a small optical fibre bundle that cannot bend over a small radius, traditional articulation cannot be used. Concentric tube robots are a relatively modern method for miniaturised actuation, capable of larger bending radii by using multiple precurved tubes, made from a superelastic material, positioned concentrically. These tubes are then translated and rotated in relation to one another causing the entire structure to deform. The advantage of this technique is the low increase in size of the modality as the wall thickness of these materials can be approximately 0.2 mm for 3 mm, diameter. However, precise control remains an issue due to the complexities of modelling multiple deformations simultaneously and solving the inverse kinematic chain in real-time.

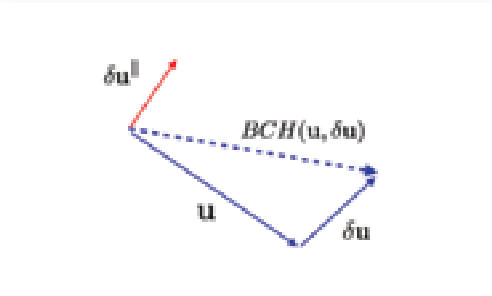
For targets in the micron scale, such as a single optical fibre; electroactive polymers or piezoelectric materials can be positioned around the fibre. By activating these in a specific sequence, the fibre can be scanned over an area. The intensity through the fibre can be measured at each position and then reconstructed to form an image. This has a distinct advantage over the normal fibre bundle used as it is capable of producing an image of considerably higher resolution.

## Mr Sebastiano Ferraris

UCL Doctoral Student (PhD)

Passion for mathematics and mathematical applications led Sebastiano to an MSc in Mathematics at the University of Turin in 2013. His dissertation topic was the investigation of new ways to use Winograd transform in Error Correcting Codes Theory. Throughout and after his studies, he had the chance to see mathematical theories applied while working as a programmer in a private company and as a developer of material flow simulation models in the automotive industry (simtec-group.eu). In summer 2014, he joined the Translational Imaging Group to work in diffeomorphic image registration under the supervision of Dr Tom Vercauteren.




**Above:** Diffeomorphic image registration.

**Below:** An alternative evaluation of the BCH formula using parallel transport.

### GIFT-Surg Focus:

In developing a thin and highly flexible instrument aimed at treating fetal disorders, the need for robust, effective and fast algorithms are crucial in image acquisition and processing. Image registration techniques are used for comparing different physiologies by estimating spatial transformations between images, as well as creating mosaics of multiple images from a fetoscope.

Image registration is applied in mosaicing to increase the field of view of the optical fibre micro camera within fetoscope. This involves combining multiple partially overlapping images into a single high resolution and deformation free composite panorama. Among multiple registration methodologies, the use of diffeomorphism (smooth isomorphism with smooth inverse) provides an interesting setting for the development of fast and robust algorithms. In particular, the log-euclidean approach proposed for the first time in 2006 (Arsigny et Al [1]), as a faster improvement to the affine invariant Riemannian approach, has found successful applications in several domains of medical imaging (in vivo mosaicing [2], brain Alzheimer detection [3], cardiac image analysis [4], mandible imaging using polyaffine registration [5]) and have been continuously improved since its introduction (Ashburner [6], Vercauteren [7], Lorenzi [8]). In this setting, computations in the Lie group of diffeomorphism are made in its Lie algebra; within this structure it is possible to easily apply calculus and statistics.

Each new step forward in the investigation of the underpinning mathematical theories involved, will find immediate application in reducing errors and computational complexity of the algorithms utilised in critical surgery.

# Mr Luis Herrera

UCL Doctoral Student (PhD)

Luis received his BSc (2010) and MSc (2012) in Computer Science from University of La Laguna in the Canary Islands. After finishing his MSc he worked in the finance sector for several months but realised that he was much more interested in research. He then enrolled in the Masters of Research in Medical Robotics and Image-Guided Intervention (2014) at Imperial College London. His MSc thesis was 'Optical Tracking for Smart Hand-Held Microsurgical Devices'. He is currently a first-year MRes/PhD student at the University College London (UCL) EPSRC Centre for Doctoral Training in Medical Imaging. He develops his work within the Translational Imaging Group (TIG) led by Prof Sebastien Ourselin.

**GIFT-Surg Focus:**

Luis' PhD work contributes to GIFT-Surg by focusing on 3D image reconstruction of fibre-optic-based photoacoustic and optical ultrasound images for image-guided fetal surgery. He is thereby intercating with both the photo-acoustics team at UCL and the mechatronics team at KU Leuven.

His work investigates the use of optical ultrasound and photoacoustic imaging probes that are scanned across the placenta to reconstruct a full 3D view of the placental volume being examined by the fetoscope. This will enable combining information from these multiple modalities and will give the surgeon a much-detailed view of the underlying vasculature and enable them to identify the surgical targets. In the short term, he is looking into compensating for the movement of the fetoscope and the placenta. This motion can create severe artefacts in the reconstructed image. However, this problem can be corrected by accurately tracking the imaging probe with respect to the placental tissue under investigation. He is investigating various approaches like using an electromagnetic tracker or image analysis methods to accurately track the probe during the procedure.

# Mr Ioannis Kourouklides

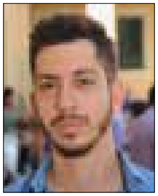
UCL Doctoral Student (PhD)

Ioannis pursued his four-year Master of Engineering degree at Imperial College London in the fields of Electronic and Information Engineering. He graduated in 2014 with a First Class Honours and his thesis involved applications of Computer Vision and Machine Learning in Mobile Robotics. In the summer of 2014, he joined the Translational Imaging Group at the Centre for Medical Image Computing for the GIFT-Surg project. He is currently funded by the Engineering and Physical Science Research Council (EPSRC) as part of the 2014 cohort of the EPSRC Centre for Doctoral Training in Medical Imaging. The reason he joined the CDT is so that he can make a direct impact on the real lives of people and especially their health. In terms of industrial experience, he had an internship with Broadcom, as a R&D Software Engineer and a six-month placement as a Software Developer at Citigroup in 2013. As a result, he managed to solidify his programming skills while working with huge legacy code as a part of a global diversified team.

**GIFT-Surg focus:**

Ioannis' research, as part of GIFT-Surg, is focused on real-time data fusion for image-guided fetal surgery. Apart from his primary supervisor and project lead, Prof Sebastien Ourselin, he is also co-supervised by Dr Tom Vercauteren, along with two clinical supervisors, Prof Jan Deprest from KU Leuven in Belgium and Dr George Attilakos from NHS University College London Hospitals. His individual project will consider new methodologies for image fusion inspired by models and concepts from Medical Image Registration, Computer Vision and Machine Learning.

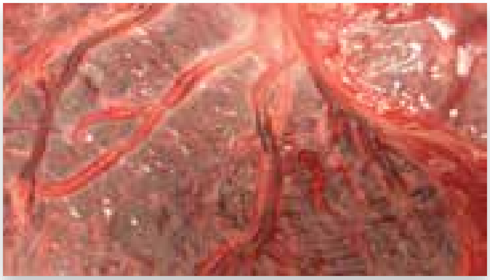
The ultimate goal of his PhD project will be the real-time feedback during therapy, based on a combination of direct vision via a very small camera (fetoscope), ultrasound, photoacoustic imaging and external ultrasound, fused with preoperatively acquired information on maternal and other relevant structures. Semi-automated and automated methods will be combined to fuse imaging modalities and models.

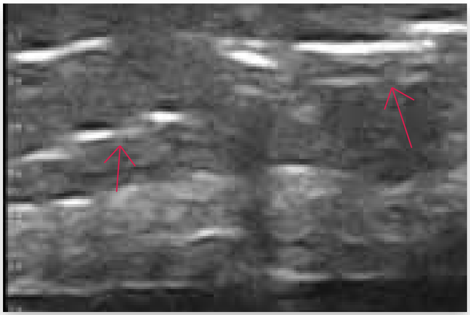


# Mr Efthymios Maneas

UCL Doctoral Student (PhD)

Efthymios is currently a MRes/PhD student at the EPSRC Centre for Doctoral Training in Medical Imaging at University College London (UCL) and a member of the Translational Imaging Group (TIG) led by Prof Sebastien Ourselin, within the Center of Medical Image Computing (CMIC). Before coming to UCL, he received his M.Sc. in Medical Informatics from the National and Kapodistrian University of Athens. his Master thesis project included simulation in the field of photoacoustics and conducted in the Biomedical Research Foundation of the Academy of Athens. He completed his B.Sc. in Biomedical Engineering from the T.E.I. of Athens which included an internship at GE Healthcare as a Field Service Engineer trainee.





**Above:** Color and Ultrasound image of ex vivo perfused placenta showing detailed vasculature (Arrows highlight the vasculature visible on the ultrasound image).

**GIFT-Surg Focus:**

Efthymios' research focuses on the development of new intra-operative imaging methods for image-guided fetal surgery. One of the main deliverables of the GIFT-Surg project will be the integration of new imaging modalities such as fiber-optic ultrasound and photoacoustic imaging to the fetoscope used for minimally-invasive surgery. These methods have never before been applied for intrauterine imaging, and as such little is known about the features of fetal and placental tissues that can be imaged using these methods. His initial aim is to apply these methods on the ex vivo human placenta to provide prior knowledge and a benchmark for the future in vivo imaging.

Initially, he will use existing systems - such as a clinical MRI system, a commercial ultrasound system, and a pre-clinical photoacoustic system - to image whole ex vivo human placentas and obtain high-resolution 3D images. The placentas will be obtained from consenting patients following normal delivery and will be perfused with an appropriate contrast agent. Subsequently, he will scan the placentas with the fiber-optic ultrasound and photoacoustic probes being developed by Dr Adrien Desjardins and Prof Paul Beard, characterise the images obtained using these novel methods with respect to the high-resolution images previously obtained, and propose and test ways to improve image quality as necessary.

## Mr Marcel Tella

UCL Doctoral Student (PhD)

Marcel studied telecommunications engineering with a special focus on image processing and computer vision in the Technical University of Catalonia (2010). His studies included working on a research project, which was undertaken at TU Vienna under the supervision of Dr Xavier Giró and Dr Matthias Zeppelzauer (2013-2014). The research project involved development of contextless object recognition using shape-enriched SIFT and bad of features model.

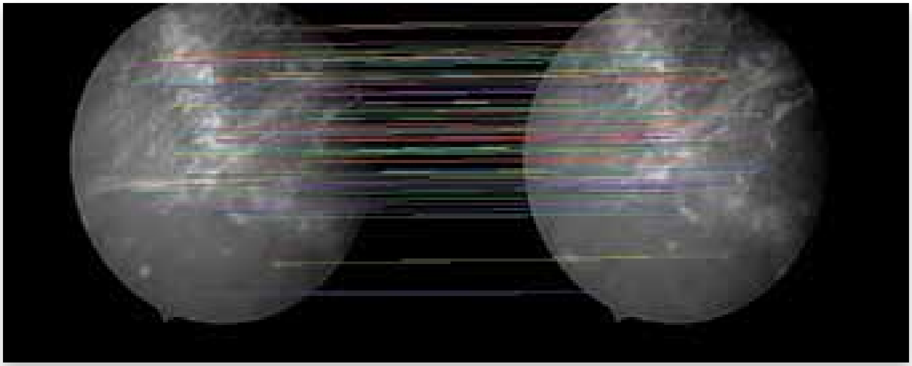
He moved to UCL in 2014 to start his doctoral work on the GIFT-SURG project under the primary supervision of Prof Sebastien Ourselin with his secondary supervisor Dr Tom Vercauteren. During his doctoral work he will be investigating mosaicking techniques to reconstruct the full placental image from limited field of view fetoscopic images.

**GIFT-Surg focus:**

A major challenge that needs to be overcome in the current TTTS surgical procedure is the limited field of view of the fetoscope. In addition, one has to also cope with optical distortions as well as imaging noise. This makes identification of the vessels that need to be targeted difficult. Mosaicking techniques are proposed in order to spatially align different images in a temporal sequence and increase the field of view.

Marcel is currently researching novel mosaicking techniques in order to obtain an image of the whole placenta as well as the 3D reconstructed image of the placenta. This will enable more efficient surgical planning and accurate localization of the surgical tools during the procedure.

This work is done in collaboration with Dr Pankaj Daga and with the help of the surgical team from KU Leuven, Belgium.



**Above:** Identification of correspondence points between video frames is a critical part of the image mosaicking algorithm. The above image shows correspondences established between fetoscopic video frames using our feature extraction algorithm.

# Mr Guotai Wang

UCL Doctoral Student (PhD)

I obtained my Bachelor and Master's degree of Biomedical Engineering in Shanghai Jiao Tong University and then joined TIG in September 2014. My research interest mainly includes medical image segmentation, registration and visualisation. During my Master's programme, I worked on segmentation framework in liver surgical planning system. In UCL, my research project is to develop algorithms for image guided fetal surgery, under the supervision of Professor Sebastien Ourselin.

**GIFT-Surg Focus:**

Planning and navigation systems are significant for ensuring the safety and success of fetal surgery. Segmentation of different fetal organs and even the whole fetus from medical images is a fundamental component for surgical planning and navigation. Detailed fetal anatomical structures can be learned from segmentation results of preoperative image data (e.g. MRI) so that an optimal surgical strategy can be achieved. During the surgery, intra-operative imaging (e.g. Ultrasound) can help to guide the localization of anatomical structures, which benefits from real-time segmentation. At the start of the project, Guotai will investigate the segmentation of placenta from MRI, which is of great significance for the laser therapy for twin-to-twin transfusion syndrome (TTTS).

**Above:** 3D rendering of an ultrasound in the womb.

## Ethical Framework

Throughout the project we will be continuously reviewing the ethical, legal and regulatory literature on innovation in intrauterine fetal surgery. We will have a service users and user-support panel as well as a multidisciplinary ethical panel to provide views on legal, ethical, philosophical, economic, and public policy dimensions.

The project also consists of a Patient and Public Advisory Group that is made up of parents, pregnant women and their spouses as well as the following charities:

ARC Antenatal Results and Choices

Bliss for babies born too soon, too small, too sick

cdh UK The Congenital Diaphragmatic Hernia Charity

Shine Spina bifida • Hydrocephalus Information • Networking • Equality

Tamba TWINS & MULTIPLE BIRTHS ASSOCIATION

Throughout the project we will be organising a number of informative public events such as stalls at science fairs, panels and exhibitions. More information on these activities can be found on our Facebook page:

**www.facebook.com/GIFTSurg**

For any further questions, comments or information please contact us at:

**GIFT-Surg-info@ucl.ac.uk**

# Selection of GIFT-Surg in the press



20 | **NEWS**

## Miniature robot hand set to revolutionise surgical treatment of babies in the womb

An automated pincer will provide 3D images of foetuses and tackle damaging conditions such as spina bifida

**by Robin McKie**
Science Editor

**ADVANCING FOETAL SURGERY**



SOURCES: EPSRC, WELLCOME TRUST

Scientists have launched a £10m project to create a tiny surgical robot hand that could transform the treatment of children with spina bifida and other congenital conditions.

The aim of the research, which is being carried out by engineers at University College London (UCL) and KU Leuven in Belgium, is to create a minuscule device that would provide 3D images of a foetus while it is still in the womb which will also act as an automated robot hand. This could carry out delicate surgery or deliver stem cells to an unborn child's damaged organs.

"The aim is to create less invasive surgical technologies to treat a wide range of diseases in the womb, with considerably less risk to both mother and baby," said the project leader, Professor Sebastien Ourselin, from the UCL centre for medical image computing.

A prime priority for the project, which is being funded by the Wellcome Trust and the Engineering and Physical Science Research Council, is to revolutionise the treatment of children with spina bifida. About one in 1,000 babies are born with myelomeningocele spina bifida, the most serious form of the condition. This is caused when the spine of an unborn baby does not form properly and amniotic fluid leaks into it. Germs in the fluid can then spread up the spinal column until it reaches the brain and inhibits its development. As a result, babies born with spina bifida often suffer severe neurological complications. The answer, doctors have concluded, is to try to patch the gap once it has appeared in the baby's spine.

Such surgery involves opening the mother's abdomen and uterus and incurs a significant risk of triggering premature birth, however. As a result, operations like these are rarely carried out. "They are very dangerous," said project manager Jenny Nery. "There is a very severe risk to the mother's health."

In addition, surgery on the unborn can only be carried out when the foetus is at least 26 weeks old. By that time, considerable damage may already have been done to the child's growing brain. "We need to find a way to block up the gap in the baby's spine at a much earlier stage in the foetus's development," added Ourselin. "Ideally, it should be done around 16 weeks. The earlier the treatment, the more effective it will be."

At present, such operations are impossible. The objective of the Wellcome-funded project is to develop instruments – based on the latest developments in optics and robotics – that will make them possible.

The engineers and doctors involved in the project envisage developing a very thin, highly flexible probe that would be inserted into the womb of a woman carrying a child with spina bifida. The head of the probe would have one strand fitted with a tiny camera that would use laser pulses and ultrasound detection – a combination known as photo-acoustic imaging – to generate a 3D photograph inside the womb. These images would then be used by the surgeons to guide the probe to its target: the gap in the foetus's spine.

The probe's other arms would also be fitted with tiny instruments which would carry a piece of gel or patch that would then be inserted over the gap in the baby's spine. "It will be like a plaster," added Ourselin. "If we can do that, there will massive gain for the foetus while there will be little risk to the mother."

At present, most designs for the robot foetal surgeon envisage a three-pronged device that has one arm fitted with a camera and two that are fitted with pincers or other instruments.

"We are still in the design stage, so we could end up with a device with four or five arms in the end," added Ourselin. "Nor would it be used merely to put in patches. It could carry out delicate surgery or deliver stem cells to damaged organs."

In addition to the spina bifida cases, the device could also help in the treatment of many other foetal conditions, such as twin-to-twin-transfusion-syndrome (TTTS) in which there is an unequal, life-threatening supply of blood twins inside the womb.

"Operating on babies in the womb should not be undertaken lightly," added Ourselin. "We need the very best surgical tools to do something like this, and this project will make sure we have them in the next few years."

**Robin McKie has been shortlisted for the 2014 journalism awards run by the Association of British Science Writers for his story 'Gene wars: the last-ditch battle over who owns the rights to our DNA'. Read the article at: gu.com/p/3f9pg**

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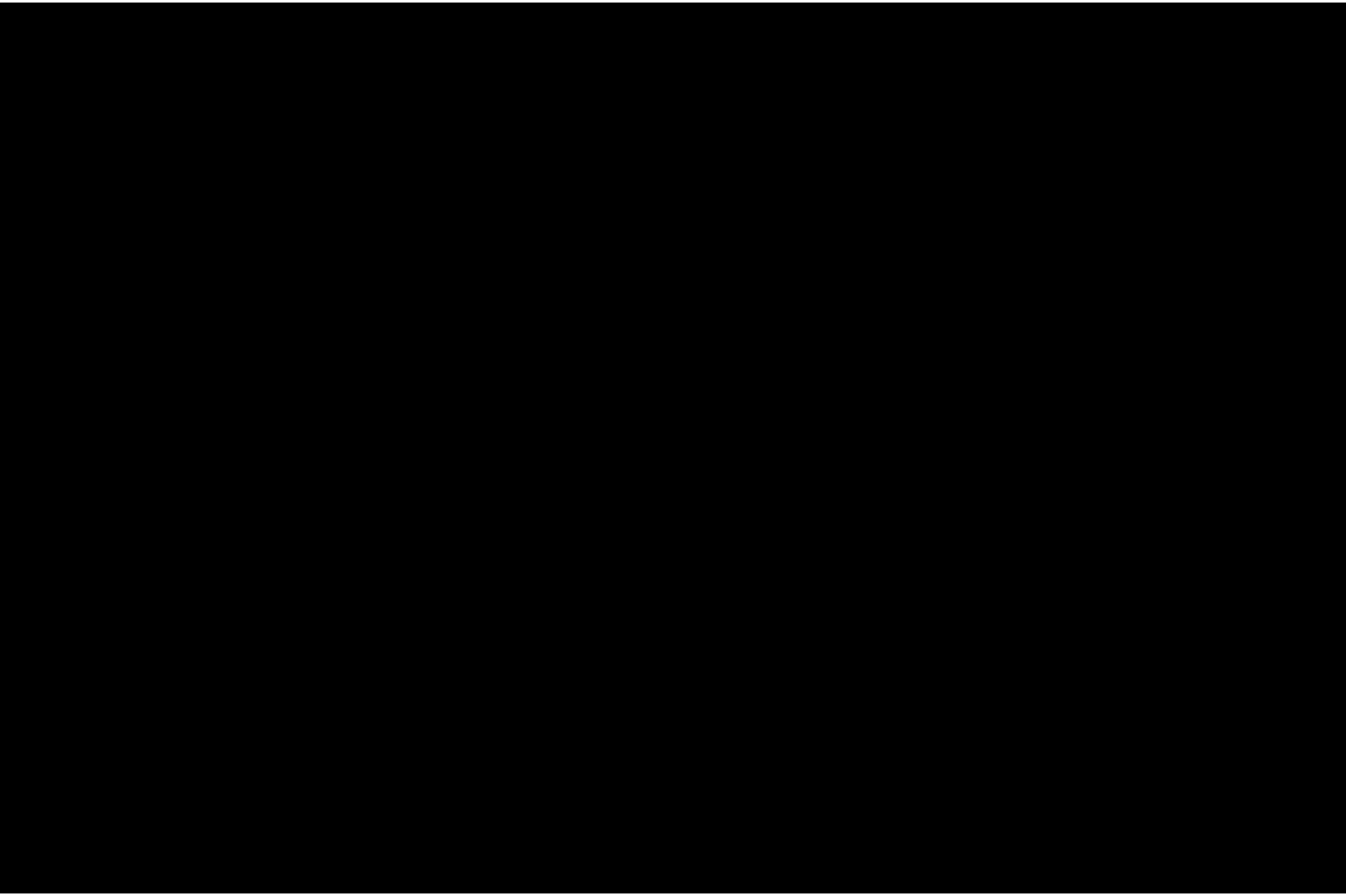
## Notes



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