Glaucoma – Advanced, LAbel-free High resolution Automated OCT Diagnostics

GALAHAD

GALAHAD project newsletter #6

January 2020

GALAHAD is a research project supported by the European Commission through Horizon 2020 under Grant Agreement 732613.

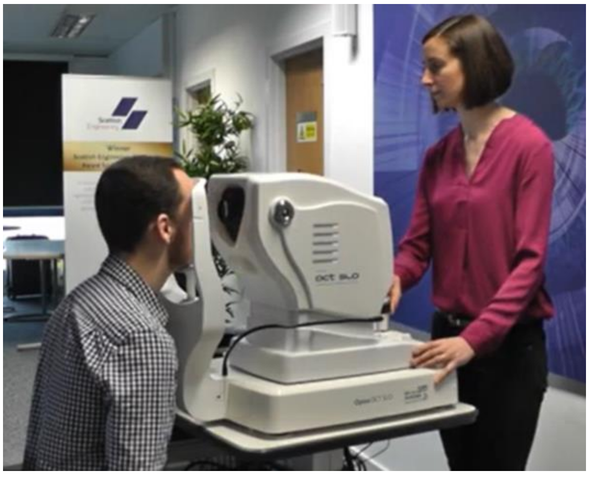
Welcome to the final GALAHAD project newsletter!

In this final edition we present:

- A summary of the project results
- An update on the automated algorithm development at UPV
- A summary of the advances in grating production at Ibsen Photonics
- Details of the 1 µm axial resolution OCT characterisation by DTU
- Application of the two GALAHAD systems on rodents (Glostrup) and humans (Optos)
- A review of the project workshop, held at the Royal Society of Edinburgh (08-Jan-2020).

More info is available on the website (www.galahad-project.eu).

GALAHAD project results overview



- NKT developed a world-beating polarised supercontinuum source (robust >25 dB PER for >2200 h)
- Ibsen has progressed a new large area grating process which will have a major impact
- Coordinator G&H set the new state-of-the-art in both SM and PM broadband fused fibre components, as well as launching many new products: PM and SM collimators, SM and PM delay lines, a motorised polarisation controller and a variable dispersion compensator.
- Algorithms were developed by UPV to automatically segment and classify layers in retinal and dermatological human OCT images. Deep learning strategies outperformed hand-driven learning approaches: this represents the new state-of-the-art in this area.
- WWU reported the first measurement of retinal refractive index as a function of wavelength with its world-class digital holographic microscopy apparatus
- The two GALAHAD PS-OCT systems were characterised with axial resolutions of 1 µm
- These systems were used for *in vivo* imaging of rats and human retinas

Dozens of conference and journal papers have been published which provide detailed technical information. Please see the website or get in touch with the email addresses below.

Gooch & Housego · optos · Universitat Politècnica de València · DTU · Gloucestershire Hospitals NHS Foundation Trust · Region H Rigshospitalet · NKT Photonics · Westfälische Wilhelms-Universität Münster · VIVID Components · Ibsen photonics

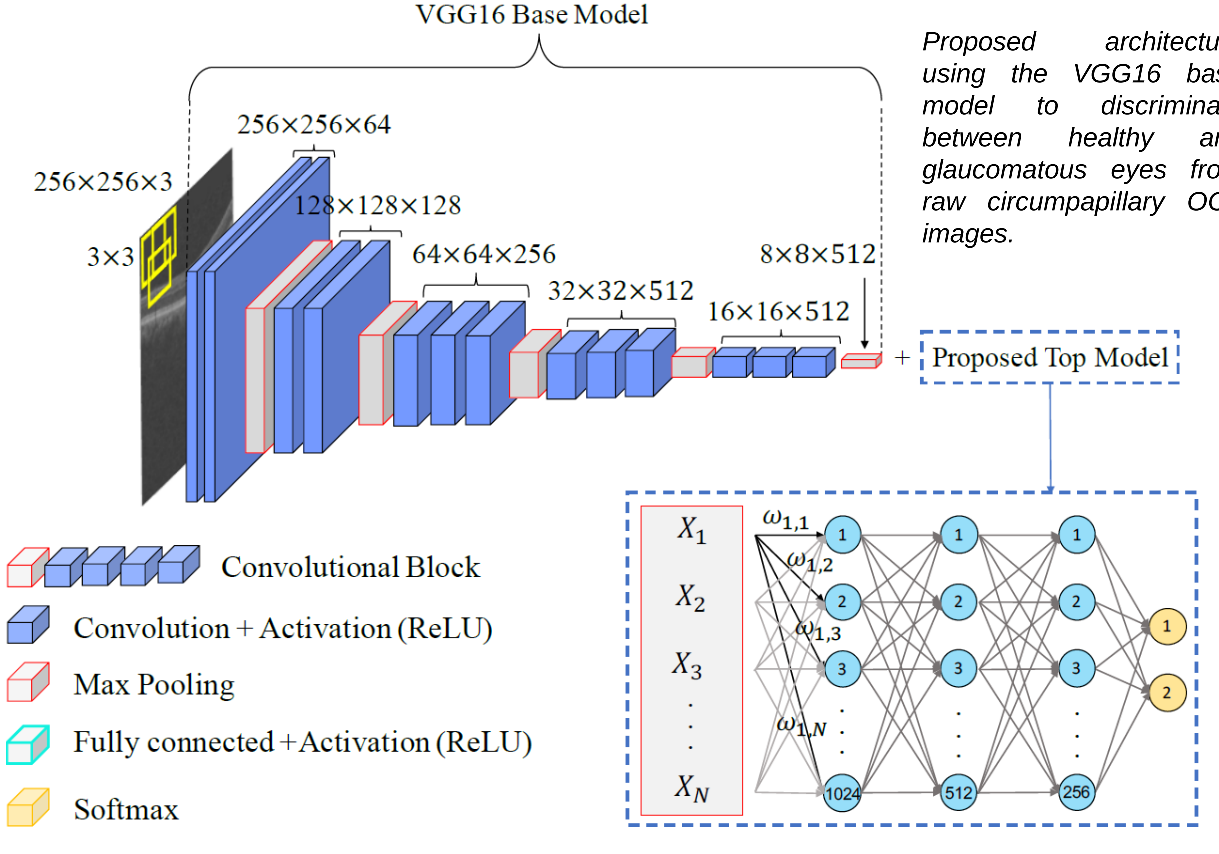
Coordinator	Liam Henwood-Moroney	lhenwood-moroney@goochandhousego.com
Admin	Bruce Napier	bruce@vividcomponents.co.uk

Automated algorithm development in GALAHAD

Engineers at UPV have developed various methods during the GALAHAD project. The best results were achieved by making use of one of the highest trending techniques in the computer vision field: deep learning. In the following pages the key results are presented.

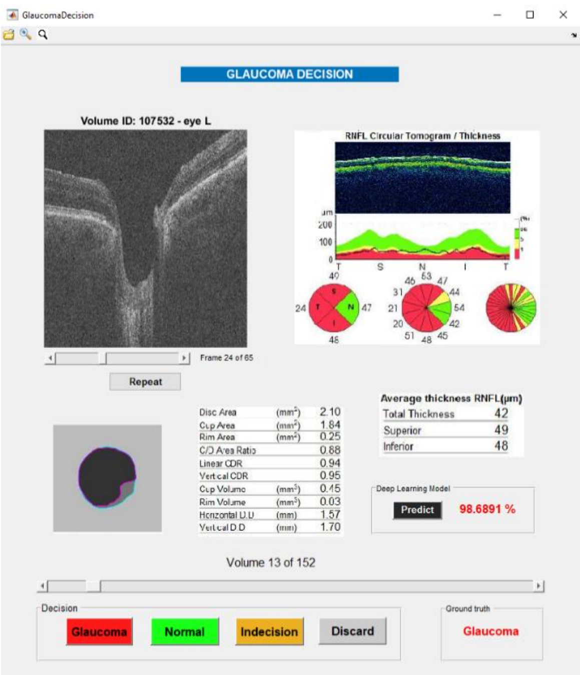
Strategy for automatic glaucoma classification from circumpapillary human OCT images
An automatic computer-aided diagnosis system able to discriminate between healthy and glaucomatous eyes, making use of only the raw circumpapillary OCT images, was successfully developed by UPV. Deep-learning techniques were attained in order to create the prediction model from the OFTALVIST database.

A fine-tuned VGG16 architecture achieved the best results to address the glaucoma classification. In particular, an accuracy of 0.96±0.02 was reached using a top model composed of three fully-connected layers with 1024, 512 and 256 neurons, followed by a softmax layer of two units corresponding to the healthy and glaucoma classes, as can be seen schematically in the diagram below.



Proposed architecture using the VGG16 base model to discriminate between healthy and glaucomatous eyes from raw circumpapillary OCT images.

Strategy for automatic glaucoma classification from SD-OCT human volumes
Currently, experts do not usually use 3D OCT scans for glaucoma diagnosis because it requires a prohibitively large workload. UPV worked under the hypothesis that OCT volumes have an unknown and valuable potential for diagnosis. For that reason, deep-learning techniques were developed to create prediction models based solely on the raw SD-OCT volumes from a database provided by GALAHAD partner GHNT.



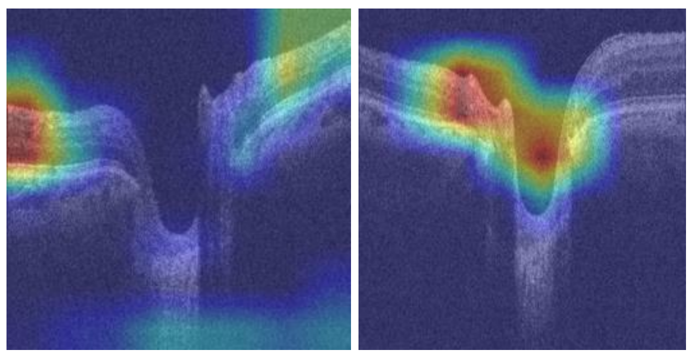
Screenshot of the application developed for glaucoma diagnosis from the OCT volumes.

The proposed model is able to discriminate between healthy and glaucomatous eyes with an accuracy of 0.81, sensitivity of 0.79 and specificity of 0.82, making use only of SD-OCT volumes focused on the optic nerve head of the retina. Additionally, Class Activation Maps (CAMs) were computed to identify the regions to which the proposed deep-learning network "paid attention" for classification. The computed heat maps allow regions of interest inside the optic cube to be identified which can be visually analysed to provide extra information for glaucoma diagnosis.

A software application for glaucoma decision was also developed (see screenshot, left). The result of the prediction model is visualized along with other OCT hyper-parameters such as normality curves for glaucoma diagnosis and C/D area ratio.

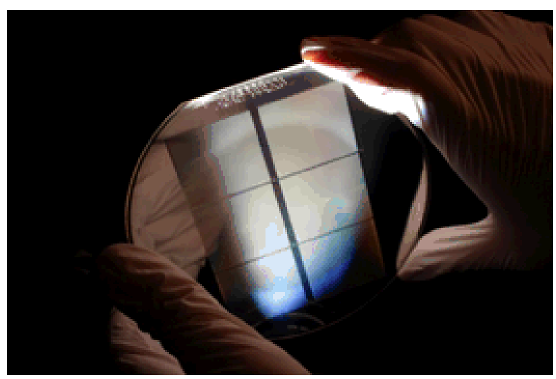
For more info contact Adrian Colomer Granero: adcogra@i3b.upv.es

Class Activation Maps (CAMs) generated by the deep-learning model to examine the differences between healthy and glaucomatous eyes. Heat maps were generated for a healthy OCT volume (left) and for one diagnosed with glaucoma (right). Note that the model focuses on the bulk retinal layers in the case of the healthy volumes, whereas regions corresponding to the optic disc cupping dominate the glaucoma class. Additionally, a characteristic peak usually appears in the neuroretinal rims, especially on the left part, of a glaucomatous volume.



GALAHAD progress in diffraction grating technology

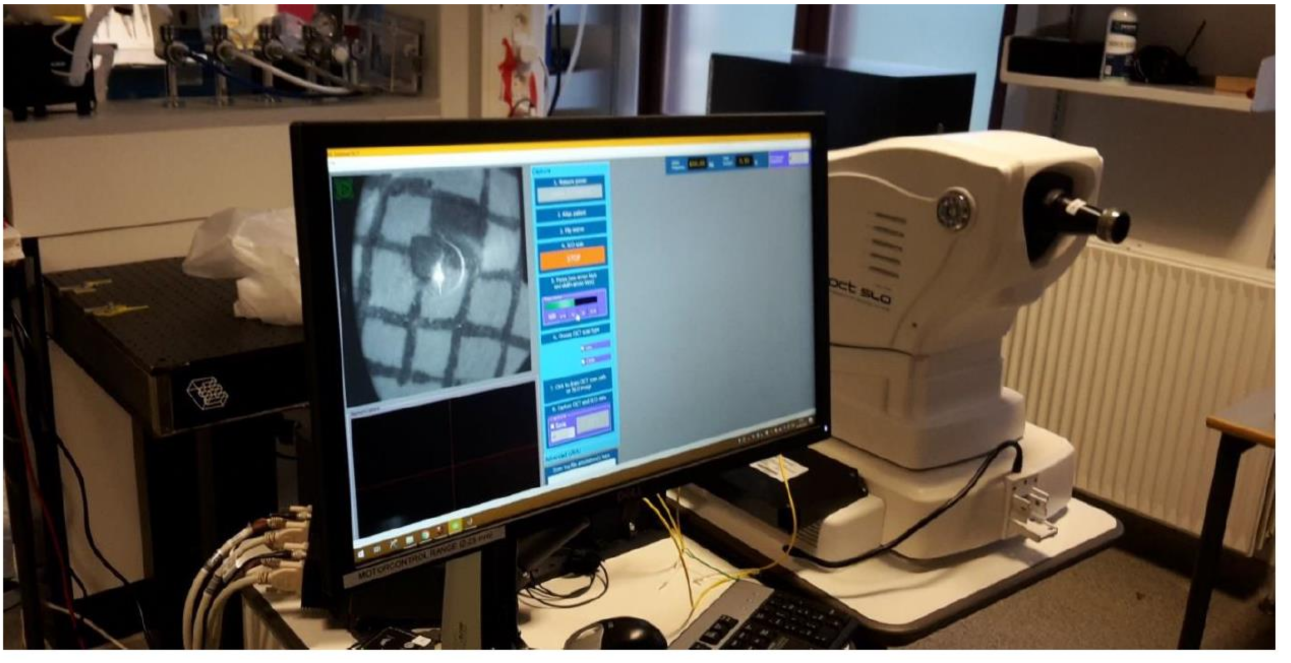
During GALAHAD, Ibsen Photonics has worked extensively with the RIE (reactive ion etch) plasma etch process for manufacturing large transmission gratings, where in-wafer uniformity and process repeatability are key. Promising results have been achieved, and will lead to a major investment in new etch equipment in 2020, which will expand Ibsen's capacity and capabilities. Use of new and optimised etch processes is expected to have a strong positive impact on Ibsen's manufacture of transmission gratings, allowing expansion of its world-leading position in gratings for OCT applications, but also for telecommunication, high power laser, and LIDAR applications.



For more info contact kristian.buchwald@ibsen.com

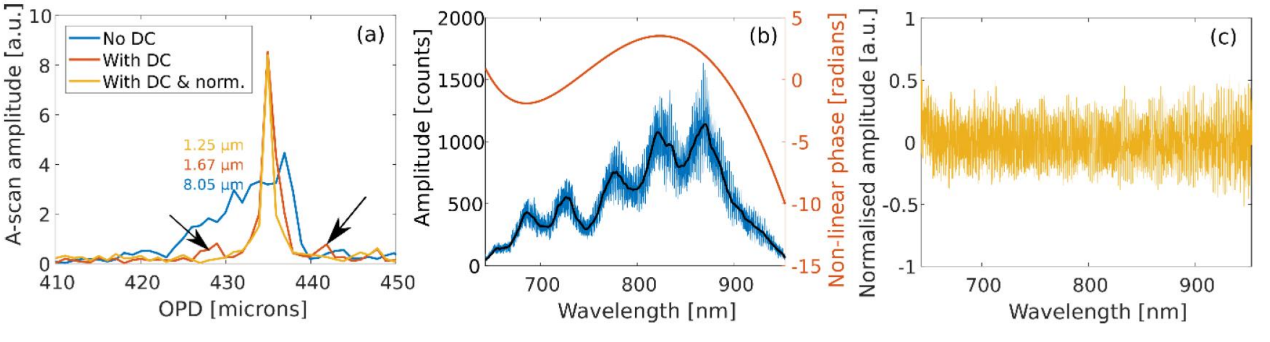
GALAHAD system characterisation

The GALAHAD-1 OCT system, which was sent to Rigshospitalet-Glostrup, was thoroughly characterised by the Technical University of Denmark (DTU) in Oct and Nov-2019. The characterisation is essentially a net evaluation of the supercontinuum source (NKT), spectrometers (Ibsen), broadband PM components (G&H) and data acquisition software (Optos) which together determine the quality of the ultra-high resolution OCT images.



The GALAHAD-1 OCT system at Rigshospitalet-Glostrup ready for system performance characterisation.

The sensitivity was found to be within the range of commercial supercontinuum-based OCT systems (~80-90 dB), but more importantly the axial (depth) resolution was found to be ***<1 μm in tissue*** making the GALAHAD OCT system capable of resolving single cells in the human body. This resolution was only possible by careful resampling and correction of the unbalanced dispersion introduced within the Michelson interferometer of the OCT system. With this result GALAHAD sets the new state-of-the-art for PS-OCT systems.

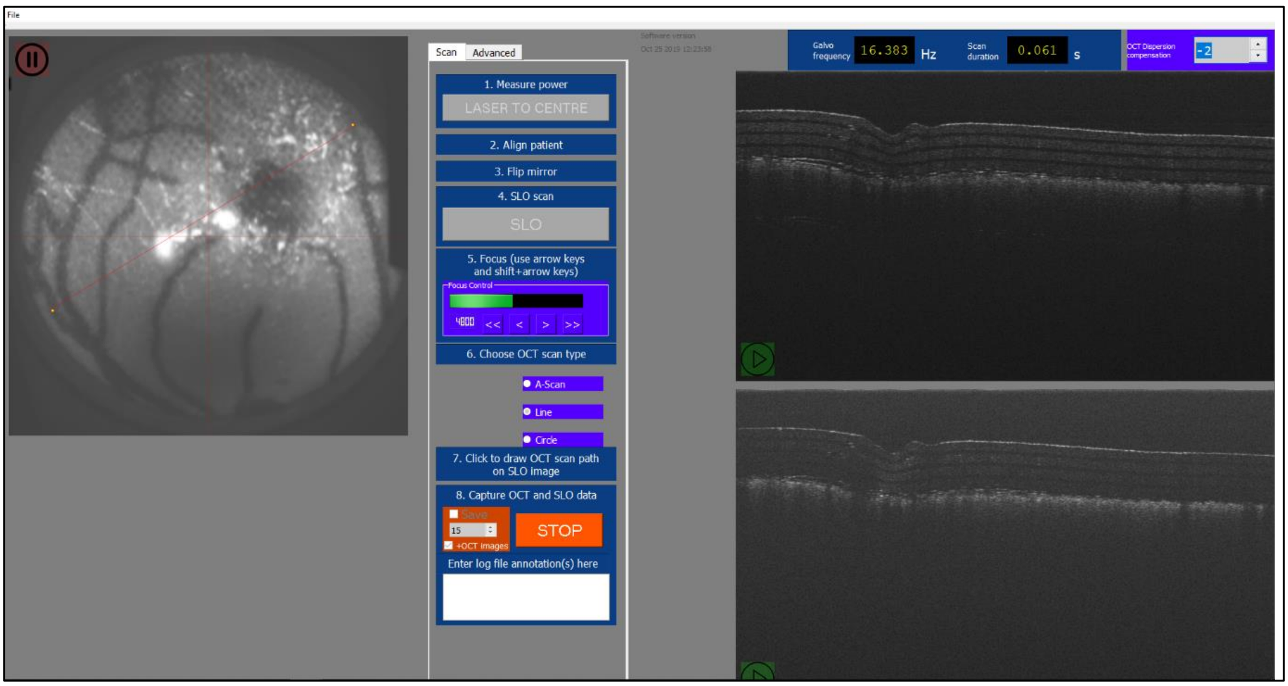


Resolution of the GALAHAD-1 system. (a) The resolution of the non-dispersion compensated A-scan (blue), the dispersion compensated A-scan (red), and the dispersion compensated and normalised A-scan (yellow). (b) The spectrum (blue), the reference (black) and the non-linear phase used for DC (red). (c) shows the normalised spectrum with a non-varying envelope.

For more info contact Niels Møller Israelsen: nikr@fotonik.dtu.dk

Application of the GALAHAD systems

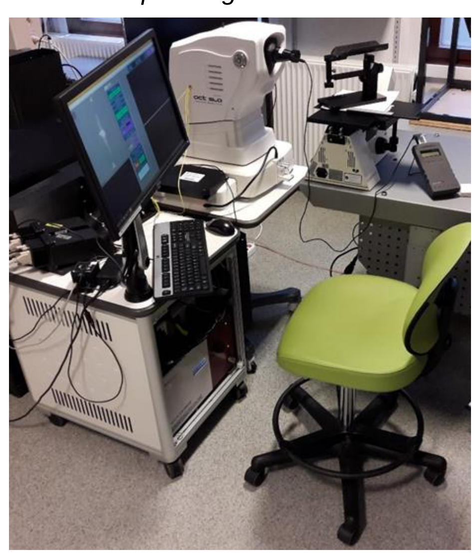
The GALAHAD systems (GALAHAD-1 and -2) were adapted from Optos' research imaging systems. The source was replaced with the NKT supercontinuum source, the interferometer with a broadband, polarisation maintaining version from G&H and the spectrometer with two Ibsen spectrometers connected via a polarising beam-splitter. The initial design was for rodent imaging, which required changes to the sample arm optics in order to reduce the beam diameter to enable imaging through a small rat pupil. A new reference arm was built with a length range large enough to enable imaging of both rat eyes and human eyes. Adjustable dispersion compensation prisms were included with a degree of travel suitable for a large range of eye sizes. Bespoke software was developed at Optos (including an online update and maintenance facility) to simultaneously acquire data from both spectrometers, enabling polarisation sensitive imaging.



The GALAHAD software being tested on a model eye "phantom". Live OCT images from both spectrometers can be seen on the right-hand side. A scanning laser ophthalmoscope image is included on the left-hand side for selecting an OCT scan area.

Delivery of the GALAHAD-1 rodent OCT system

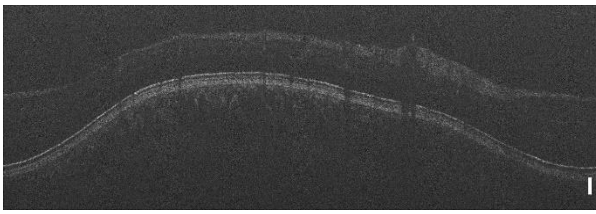
The work of the hardware partners in the GALAHAD consortium culminated in the delivery of the first OCT system from the project (GALAHAD-1) to Rigshospitalet-Glostrup for rodent imaging experiments. This was successfully installed and commissioned in Aug-2019. Glostrup and Optos have worked together to develop a user interface that has enabled easy data collection. The characterisation at DTU (see previous page) was in good agreement with the in-house testing at Optos.



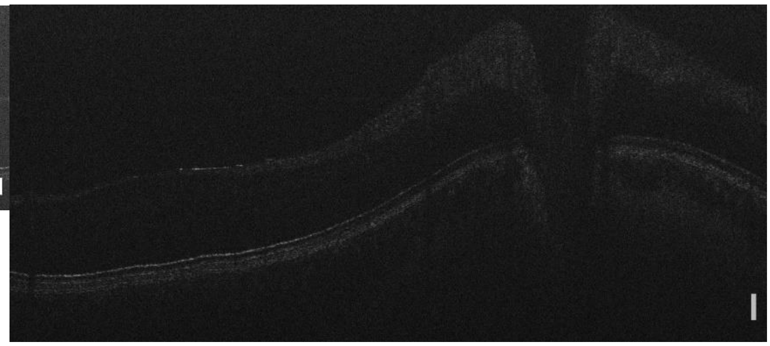
The complete GALAHAD-1 system, delivered and installed at Glostrup, ready for rodent imaging experiments.

Human retinal imaging with GALAHAD-2

Following the success of early rodent imaging sessions, the second GALAHAD device was assessed for suitability for human imaging. Safety and ethical criteria were met, allowing limited human tests on informed volunteers to take place. These resulted in high resolution OCT images of the human retina, such as those shown below. The high axial resolution is apparent, although the signal is lower than in a commercial system. Single images are shown as eye movement prevents averaging in these tests.



Example high resolution images of a human volunteer taken with a GALAHAD OCT device. The scale bar shows a depth of 100 µm. The images are single circular scans.



For more info contact: Margaret Normand MNormand@optos.com

GALAHAD workshop and demo held a Royal Society of Edinburgh

The grand surroundings of the Royal Society of Edinburgh provided the perfect venue for the final GALAHAD workshop and demonstration (WED 08-Jan-2020). Over seventy attendees came to the event, including clinicians, OCT technologists and Ph.D. students. Visitors were also treated to the chance to see some of James Clark Maxwell's original notebooks and papers. The presentations from GALAHAD team members were very well received, and the live demonstration by Margaret Normand and Jamie Foubister from Optos provided a fitting end to the project. Some of the presentations are available from the project website:

https://galahad-project.eu/events/galahad-workshop

A series of presentations on the project results was presented (left) and the workshop culminated in a live demonstration of the GALAHAD system on a human subject (right).