2017 has been a busy year for everyone at the QSMSC! Many studies have been concluded and published, but many more projects are still ongoing with even more ready to start. 2018 is going to be a very exciting year, and we will finally find out the results of the MS-SMART trial at end of the year. Recruitment for two more trials in secondary progressive MS (MS-STAT2 and MS-OPT) will also begin. However, QSMSC research is not limited to clinical trials! Physicists and research fellows are investigating advanced MRI techniques, post-mortem tissue, and the oral microbiome to find surrogate biomarkers of disease activity, neurodegeneration, and neuroprotection. Furthermore, the team is increasing its collaborations with other departments and groups, helping to improve the care of paediatric patients and symptoms treatments.

The QSMSC team is working hard, but its efforts would be in vain without the participation and passionate collaboration of the patients and volunteers that agree to be involved in our studies. Therefore, thanks to all the participants who are making our research a success!

The QSMSC team wishes everybody a Merry Christmas and a Happy New Year!

In collaboration with (amongst many others)

UK MS REGISTER
www.ukmsregister.org

MS Society
www.mssociety.org.uk

National MS Society
www.nationalmssociety.org

Shift MS
www.Shift.ms

MS TRUST
www.mstrust.orh.uk

Contact Us at
uclh.qsmsc@nhs.net
Or Call
0203 108 1955

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www.qsmsc.info
Every year, in Europe, experts in the field of MS meet to discuss and show their findings in treatment to better understand the disease. This year, Paris hosted the 7th Joint ECTRIMS - ACTRIMS Meeting. Our researchers and PhD students were amongst the 10,000 who attended this important conference, contributing more than 15 aspects of our work as oral or poster presentations. Abstracts and podcasts from the whole event are freely available at the “ECTRIMS online library” website. (onlinelibrary.ectrims-congress.eu)

Research on Spinal Cord

Dr Bhavana Solanky is working on advanced MRI techniques investigating the associations between tissue sodium concentration and spinal cord injury.

Dr Marcello Moccia along with Dr Ferran Prados is involved in developing accurate and precise longitudinal measurements of spinal cord atrophy in MS. They are developing the first segmentation-based technique for spinal cord atrophy measurement, the GBSI (generalised boundary shift integral) on behalf of the ECTRIMS-MAGNIMS group.

Dr Francesco Grussu and Marco Battiston have been busy developing new techniques to study spinal cord tissues in-vivo, such as neurite orientation dispersion (NODDI) and qMT.

Follow up Research on Clinical Isolated Syndrome

Dr Wallace Brownlee and Dr Karen Chung and their mentors Prof. Miller, Prof Ciccarelli and Dr Chard have worked on two long-term follow-up studies in Clinically Isolated Syndrome (CIS). Dr Brownlee showed that the development of new spinal cord and infratentorial lesions may provide important prognostic information in patients with early relapse-onset MS and their future transition to the secondary progressive stage. Dr Chung found that 31 out of 80 patients known to have MS after 30 years from their CIS had no or mild physical disability. This suggests that it is not uncommon for people with relapse-onset MS to have only mild or no physical or cognitive dysfunction in the long-term.

Dr Rosa Cortese and Dr Ferran Prados are analysing the MRI scans acquired by Dr Brownlee, looking at the predictive role of the “evanishing lesions” in clinical disability after 15 years from the CIS onset.

Technology Applications and Advanced MRI Analysis

Sarah Alexander, a Research Associate (engineer), is looking at technology solutions to help improve MS health management, and clinician outcome measures.

Almudena Garcia Gomez is part of the QSMSC Trials Office team involved in the advanced neuroimaging analyses of scans coming from multi-centre clinical drug trials in MS sponsored by industry, medical charities and academic institutions. She works with Philippa Bartlett and Jonathan Stutters under the supervision of David MacManus.
The UK MS Society has awarded funding for a research project led by Prof Claudia Gandini Wheeler-Kingshott, Prof Olga Ciccarelli and Dr Rebecca Samson. In this project, new MRI methods will be used to gain greater understanding of underlying pathological processes relating to clinical progression of people with MS. Progression in MS results in disability and causes a lot of uncertainties in people with MS. The study will enable selection of appropriate methods for monitoring the effects of treatment in clinical trials as well as potentially identifying new targets for treatment. Ultimately, the indices calculated with the proposed imaging protocol may also be included in automatic classifiers to predict progression. 50 people with early stage secondary progressive MS and 20 non-MS controls will be clinically assessed and have an MRI scan of their brain and spinal cord. Comparison will then be done with identical test done 18 months later.

**Simvastatin and Perfusion**

Dr Jeremy Chataway and co-investigators in the UK are almost ready to start the recruitment for the MS-STAT2 trial co-funded by NIHR and the UK & US MS Societies. This is a phase 3 randomised, double-blind, clinical trial investigating the effectiveness of repurposed simvastatin compared to placebo, in slowing the progression of disability in secondary progressive MS. More than 1000 patients with secondary progressive MS will be recruited in the UK. There is currently no approved treatment for secondary progressive MS. However, the phase 2 MS-STAT trial showed that simvastatin could decrease brain volume loss over two years and this provides the rationale for this larger phase 3 trial that will definitely clarify the role of simvastatin as a neuroprotector in secondary progressive MS.

The mechanisms by which simvastatin is able to protect neurons and axons is not fully understood. To investigate these mechanisms, Dr Rosa Cortese supervised by Dr Richard Nicholas and Prof. Olga Ciccarelli along with Prof John Greenwood and colleagues at Moorfields will soon be recruiting to the phase 2, placebo-controlled **MS-OPT study**. Forty people with secondary progressive MS will be recruited at UCL and will be followed up for 5 months. They will have advanced MRI, clinical, and ophthalmological investigations.

Dr Arman Eshaghi has carried out a multi-centre study on behalf of the MAGNIMS-ECTRIMS group aiming at investigating regional tissue loss in MS. He longitudinally analysed the MRI scans of more than 1200 patients with MS and found that deep grey matter volume loss drives disability accumulation in MS, and that temporal cortical grey matter shows accelerated atrophy in secondary progressive MS.

**Research on Progressive MS**

Dr Floriana De Angelis and Dr Nevin John are working on the final collection and analyses of the MRI and OCT data from the MS-SMART Cohort. Advanced MRI analysis such as MTR and Spectroscopy are being used to investigate neuroprotection in SPMS. MS-SMART is a multi-arm, double-blind, placebo-controlled trial. 445 patients were enrolled in the UK, from December 2014 to June 2016. The follow-up assessments are still ongoing and the last trial visit will occur in May 2018. So far, about half of the subjects have completed the last visit of the trial. The team at Queen Square is analysing the data and will provide the main trial results by the end of 2018.

Dr Alberto Calvi and Dr Ferran Prados, with the supervision of Prof Frederik Barkhof, are working on the analysis of slowly evolving lesions (SELS) believed to be the in-vivo representation of the smouldering plaques seen post-mortem by pathologists. The SELS have the potential to become a marker of neurodegeneration as they have been found more frequently in progressive MS patients. In this project, the QSMSC researchers will develop a pipeline to identify SELS in a large number of MRI scans from people with secondary progressive MS.

2. Eshaghi et at, Annals of Neurology (in press)

3. Slowly evolving lesions (SELS) and Jacobean maps.
The human brain can be modelled as a complex network and metrics obtained from diffusion-based structural networks can provide useful biomarkers for disease prognosis. Dr Carmen Tur, Thalis Charalambous, Dr Sara Collorone and Dr Ahmed Toosy have been working on structural connectivity, particularly in CIS patients and PPMS. Damaged pathways interrupt the communication between brain regions, and this disruption can be captured in the network of brain connections. Elizabeth Powell is also using graph theory to model white matter pathways as a network of connections in MS and non-MS brains.

![Image](image_url)

4. This is the study pipeline that Dr Tur and colleagues used to obtain the network parameters at each time point and the changes over 1 year. For each parameter and time point, and for each parameter change, 1000 bootstrap samples were used to compute the 95% Confidence Intervals.

Dr Castellazzi is one of the new recipient of the ECTRIMS post-doctoral fellowship. She is going to work on a project exploiting machine learning and rs-fMRI to develop a clinical decision system that can be used to automatically classify MS. The aim is to demonstrate the ability of rs-fMRI to characterise functional connectivity alterations in MS, and that these alterations can be used as biomarkers to differentiate MS subtypes and predict clinical progression. Adnan Alahmadi, involved in a PhD project on functional MRI, showed that cerebellar organization involving all grey matter structures reflect functional segregation in the cortex.

**Research Support**

QSMSC research would not progress without the ‘down to earth’ administration and organisation of the support team.

The Research Nurses provide clinical support to over 20 studies. Including both commercial and Investigator lead studies of Investigational Medicinal Products (IMPs) as well as supporting recruitment to the MRI and registries studies. Along with the Research Associates and Research Support Assistants they form the Research Support Team under the responsibility of the Research Manager for the co-ordination of study setup, patient recruitment, follow-up visits, data management and all aspects of patient care whilst on our studies.

Last but not least, the physics team is core to the working of QSMSC research. Biomedical Engineers, Computer Scientists, Statisticians, Neurobiologists and Radiographers are all part of this multidisciplinary team. They are working on implementing and adapting MRI scans for the specific tissue damage in MS. All the studies described above have been possible because of the work of this team, who also collaborated with many other departments and institutions in many countries!

Dr Marios Yiannakas is the head radiographer of the Unit, essential in the development and optimisation of MRI protocols for our studies. He is involved in a project focused on studying the neural pathways essential for the functioning of the legs and the lower urinary tract in collaboration with uro-neurology expert Dr J Panicker.

Dr Ferran Prados is a central figure in our group, involved in several of the above-projects. He is currently a ‘Guarantors of Brain’ fellow working in the Translational Imaging Group (TIG). His main focus is currently on developing a pipeline to analyse spinal cord atrophy in MS.

Antonio Ricciardi is working on analysing multi-modal quantitative MRI data using machine learning, in order to find the biophysically meaningful features that best distinguish among MS phenotypes.