Case for Support: CCP SyneRBI

The UK continues to be at the forefront in biomedical (i.e. preclinical and clinical) imaging with several world-firsts in integrating multiple modalities in one imaging system. Our current CCP for synergistic reconstruction with positron emission tomography (PET) and magnetic resonance (MR) imaging has brought together the best of the UK's PET and MR image reconstruction expertise. This network and its open source software form an excellent foundation for the proposed expansion into other imaging modalities, and translation of the research-enabling software to now also bring benefit to biomedical researchers. To reflect these ambitions, this proposal renames CCP PETMR to the **CCP on Synergistic Reconstruction for Biomedical Imaging (SyneRBI).**

Part 1: Track Record

The team of investigators is composed of representatives from the current CCP and Software Flagship joined by Ehrhardt to forge closer connections with the applied mathematics community.

Principal Investigator

Prof. Kris Thielemans (h-index 29, citations 3475 (Google Scholar)) is Professor in Medical Imaging Physics at **UCL** and the PI of CCP PETMR (EP/M022587/1) and its Software Flagship (EP/P022200/1). He obtained his PhD in Theoretical Physics but switched in 1997 to medical imaging. He (co-)leads many Open Source Software (OSS) projects including *Software for Tomographic Image Reconstruction* (STIR) [Thi15] which will have its 20th anniversary in 2021 (approx. 400 citations). STIR is the only OSS that allows quantitative image reconstruction for PET and SPECT data. Dr Thielemans worked in industry from 2001 to 2011 and joined UCL in 2013 with research covering all aspects of quantification in molecular imaging, often in collaboration with industry. Dr Thielemans holds 17 patents (1 pending). Dr Thielemans will be awarded the *IEEE Medical Imaging Technical Achievement Award* for "Contributions to the development of novel computational techniques and software for quantitative image reconstruction in PET and their translation to clinical practice". He has been Chair of the CoSeC Steering Committee since 2019.

Co-investigators

Dr. David Atkinson (h-index 42, citations 5754 (Google Scholar)) is a Reader in MR Imaging at **UCL** developing new MRI acquisition and reconstruction techniques to aid in clinical imaging and research. He is an author on the paper defining the international de-facto standard for MR raw data used in reconstruction. DA understands the links between PET and MRI and has publications evaluating PET/MR motion correction techniques on PET/MR cancer patients.

Dr. Matthias J. Ehrhardt (h-index 8, citations 353 (Google Scholar)) is a Prize Fellow at the Institute of Mathematical Innovation, **Univ. of Bath**. He was awarded a Leverhulme Early Career Fellowship on Machine Learning for Image Reconstruction in 2019. He is CoI and Bath-lead on grant EP/S026045/1 which aims to improve Localisation, Diagnosis and Quantification in Clinical and Medical PET Imaging with advanced mathematics.

Dr. Julian Matthews (h-index 28, citations 2738 (Google Scholar)) is a Senior Lecturer at **Univ. of Manchester**. His interests include the development of improved PET image reconstruction algorithms and the application of PET scanning in oncology, neuroscience and pharmacology. He is CoI on a PET-MR grant in dementia (EP/M005909/1), chief investigator for the clinical study being performed as part of the Dementias Platform UK partnership grant (MR/N025792/1) and involved in the optimal use of the PET-MR scanner in Manchester. His research career of 25 years has included positions both in academia and in industry (SmithKline Beecham/GlaxoSmithKline).

Prof. Andrew J. Reader (h-index 30, citations >3840 (Google Scholar)) is Professor of Imaging Sciences at **KCL**, an expert in PET image reconstruction and analysis, and a pioneer for several advances including 4D image reconstruction. His more recent research has focused on synergistic PET-MR and multi-contrast MR reconstruction, with current emphasis on integration of image reconstruction with artificial intelligence (AI). He is a Co-I for the £12.1 million Wellcome Trust / EPSRC Centre for Medical Engineering (NS/A000049/1). AJR has collaborations with industry.

Dr. Charalampos Tsoumpas (h-index 23, citations 2111 (Google Scholar)) is a Lecturer in Medical Imaging at **Leeds Univ.** since 2013 covering both clinical and preclinical aspects, Royal Society Industry Fellow with Invicro and Visiting Assistant Prof. at Mount Sinai, New York to support their PET-MR research activities. ChT is PI of an MRC project (MR/M01746X/1) on PET-MR reconstruction. Throughout his career a significant part of his research has involved STIR.

UK and International Environment

Over the period of the current CCP, the UK has invested heavily in PET-MR systems with five new systems now installed (Manchester, Edinburgh, Imperial (at Invicro, previously Imanova), Cambridge, Newcastle) in addition to the original two (UCL, KCL), and construction is underway for an eighth system in Sheffield. Substantial funding was obtained for the Dementias Platform UK (DPUK) initiative that links most of the sites. Our proposal is supported by representatives of all 8 UK PET-MR sites and by key members of the PET/CT and SPECT/CT UK community, including preclinical imaging, e.g. Leeds has access to Bruker preclinical PET/SPECT/CT and MR in the same imaging suite. This proposal seeks to extend the software towards use in (pre)clinical research, which has been received enthusiastically with several NHS clinical scientists and biomedical researchers committing to join our Steering Panel (SP). We continue to work closely with the *CCP for Tomographic Imaging* (CCPi), which focuses on *non-medical* image reconstruction and analysis with an emphasis on X-ray CT, bringing in expertise in optimisation and tomography. The collaborative efforts with CCPi will be increased and strengthened as part of this renewal.

UK academics who have expressed strong interest and will join the SP are:

> **UCL**: *Simon Arridge* (inverse problems and AI methods for image reconstruction), *Brian Hutton* (nuclear medicine, PET-MR and SPECT-MR), *Jenny Steeden* (MR reconstruction and AI, interfacing to clinical systems), *Geoff Parker* (quantitative MR and software pipelines for translation and data processing), *Jamie McClelland* (motion estimation and modelling and translation of research in radiotherapy (CoI Advanced RadioTherapy NETwork)); **UCLH**: *Anna Barnes* (PET-MR and whole-body MR imaging); **KCL:** *Paul Marsden* (PET-MR instrumentation and clinical trials), *Claudia Prieto* (MR motion correction and reconstruction), *Mattia Veronese* (PET kinetic modelling, neuro-imaging applications), Lefteris Livieratos (SPECT quantification), *Jorge Cardos*o (AI methods for image analysis); **Leeds**: *Alex Frangi* (computational medicine), *Daniel Lesnic* (inverse problems), *Robert Aykroyd* (Bayesian methods & image analysis); **Cambridge:** *Tim Fryer* (PET physics and kinetic modelling, PET-MR motion correction), Martin Graves (cardiovascular MR, imaging standards); **Cardiff:** *Hannah Chandler* (development and validation of novel PET/MRI methodology and analysis pipelines for clinical translation); **Edinburgh:** *Edwin Van Beek* (imaging to study cardiovascular and lung diseases), *Giorgos Papanastasiou* (PET-MR image analysis), *Catriona Wemberley* (PET kinetic modelling and simulation); **Newcastle:** *Ross Maxwell* (pharmacological imaging of cancer); **Sheffield:** *Jim Wild (*hyperpolarized MR, pulmonary MR)*, Steven Sourbron* (MR kinetic modelling, leading the ISMRM Open Source Initiative for Perfusion Imaging); **ICR**: *Simon Doran* (imaging informatics); **Surrey:** *Nikolaos Dikaios* (PET and MR reconstruction and motion correction, proton CT reconstruction, STIR expertise); **CCP for Tomographic Imaging** (CCPi) representatives

Importantly, we also have strong connections with numerous **industrial partners** (see Letters of Support), including the UK **National Physical Laboratory**, **Invicro (formerly Imanova), GE Healthcare**, **Siemens Healthineers**, **Philips UK**, **Bruker, MEDISO Medical Systems** and **Leeds Test Objects,** many of which will have representatives on the SP.

Our current CCP PETMR has generated **international interest**, with particularly active contributions to the software from Germany and Australia. Current commitments to join the SP include: *Christoph Kolbitsch* (**PTB** Berlin (D), MR quantitative imaging, PET-MR reconstruction and motion correction); *Ronald Boellaard* (**VUmc** Amsterdam (NL), PET reconstruction and clinical trial standardisation); *Simon Rit* (**CREATIS** Lyon (F), Cone-Beam CT and SPECT reconstruction, leading the OpenRTK open source project) and *Zahi Fayad* (Mount Sinai Hospital, cardiovascular PET-MR applications).

Furthermore, we have two international External Advisors of the highest possible reputation:

- ***Jeffrey Fessler*** (Univ of Michigan, USA) is a world-authority in developing new image reconstruction algorithms and analysing their theoretical behaviour. Uniquely, his contributions continue to lead the PET, CT, SPECT and MR reconstruction algorithm field.
- ***Ciprian Catana*** (Harvard Medical School, USA) is trained in both radiology and biomedical engineering and leads the PET-MR field in testing new methods in a clinical setting.

Part 2: Proposal and context

Motivation and background

Imaging has a crucial role in biomedical research, drug development and medical diagnosis. Our current CCP on synergistic reconstruction for PET-MR (CCP PETMR, www.ccppetmr.ac.uk) has created a network of UK and international researchers working towards the beneficial integration of image reconstruction of multi-modal data from PET-MR scanners. Synergistic PET-MR image reconstruction exploits the fact that both datasets are derived nearly simultaneously from the very same patient, using the rich cross-modality information during the reconstruction of both the PET and MR images. Our network and software have placed the UK at the forefront of the drive towards optimised reconstruction of PET-MR images. We now propose a significant expansion to other modalities and the biomedical arena, to form CCP SyneRBI, as will be detailed below.

Highlights of achievements of CCP PETMR

Software

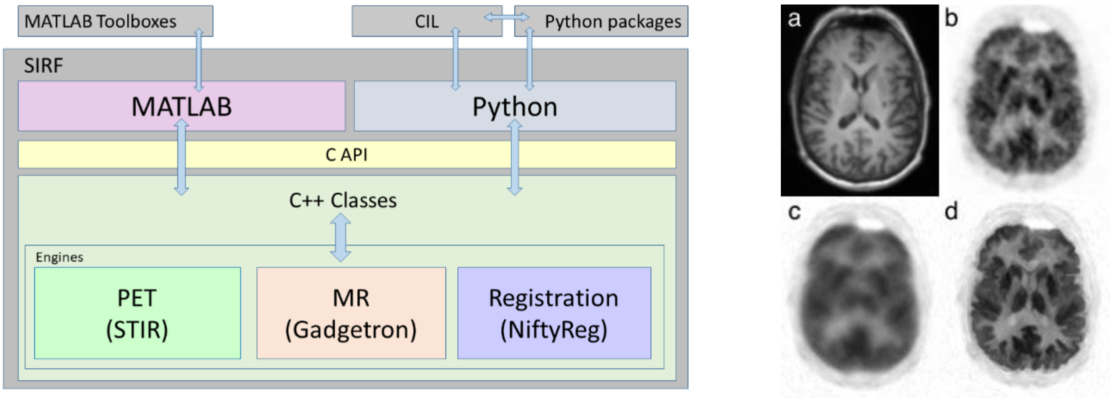

*Fig. 1. (*adapted from [Ovt19]) *Left.* Architecture of SIRF showing C++ core framework library with interfaces to external OSS packages for underlying functionality ('engines'), MATLAB/Python interfaces for rapid development and combination with packages available (such as the CCPI *Core Imaging Library* CIL). *Right.* Example SIRF reconstructions from brain PET-MR data. a) MPRAGE MR, b,c,d) PET reconstructed with various algorithms where *d* used information from MR.

Our current network produces high-quality open source software (OSS), see github.com/CCPPETMR/, with the *Synergistic Image Reconstruction Framework* (SIRF, Fig. 1 [Ovt19]) being the main output. SIRF provides researchers with an enabling platform to develop and test novel algorithms on PET-MR patient data, eliminating the significant technical challenges when interfacing with manufacturer's data and proprietary software. Furthermore, SIRF has proven to be an effective tool for training the next generation of researchers. SIRF can reconstruct images from both commercial clinical PET-MR systems (Siemens and GE) with various synergistic algorithms currently being integrated. Many of the software developments were contributed by members of the network, with major contributions in progress, such as the simulation framework under development at PTB (Germany) for cardiac PET-MR studies [May2019]. We also have joint software development with the CCPi on advanced optimisation and regularisation methods, and software deployment mechanisms.

Networking activities

The CCP PETMR community currently consists of about 100 researchers in PET-MR image reconstruction. Software developer meetings (every ~2 months, attended by ~15-25) often include presentations from international researchers or developers (such as in our recent 24th meeting on algorithms and software for image reconstruction with machine learning). Four hackathons (each attended by ~8-15 contributors) combined training, software development and community building (25 different attendees in total). We have co-organised seven half or one day training events (total attendance ~450) covering PET and MR principles, image reconstruction algorithms and use of SIRF. Visits funded by our Exchange programme for Early Career Researchers (ECRs) (6 completed, 3 more scheduled, durations of 1-8 weeks) result not only in joint conference/paper submissions and software contributions, but also help develop future leaders (such as J. Mayer, a PhD student at PTB, Germany, who lead the MR SIRF training at our Training School at PSMR

2019). We have organised two workshops (each attended by ~75), and will hold a 2-day Symposium for Synergistic Reconstruction (100 attendees including world experts) followed by a 2-day training school (50 attendees) in November 2019, jointly organised with CCPi. CCP PETMR has currently contributed to 7 published journal papers and 20 conference contributions, with several more either submitted, e.g. [Ovt19], or in preparation.

Links with other CCPs and CoSeC. We work closely with CCPi including joint networking events, in addition to the joint software development mentioned above. We closely interact with CoSeC Software Outlook with suggestions for projects and feedback on progress.

Unaddressed needs and opportunities

It is being increasingly recognised and demonstrated that information from complementary modalities, and from multiple time points, can be successfully combined to deliver image quality benefits compared to conventional independent processing. The capabilities of *PET-MR hardware* are projected to continue improving (e.g., improved Time-of-Flight PET resolution, advanced physiological monitoring, new MR sequences), and organ-dedicated systems (e.g. for the brain) or pre-clinical systems are either available already or under development. All such advances necessitate ongoing updates of our SIRF software. Furthermore, *spatial alignment* and *changes over time* in image contrast due to biological processes, and the associated opportunities for a synergistic framework (currently being explored in our Software Flagship) will need further ongoing support. Crucially, our software will also need to be able to handle datasets acquired at different time points [Ell17] (e.g. longitudinal imaging for treatment monitoring, pre/post intervention scans for drug development). Many of the methods developed in our Software Flagship are suitable and now ready for extension towards *multi-time point scans*. New applications such as the *MR Linac* and *MR assessment of proton beam therapy* are creating more opportunities.

New multi-modality systems are now available or under development, for instance in combination with single photon emission computed tomography (SPECT), a modality for which reconstruction algorithms are very similar to PET, but with different needs for acquisition modelling. UCL is currently testing a *world-first prototype* for a clinical *SPECT-MR* scanner [Hut19], with prototype preclinical systems available. The recent Mediso AnyScan clinical system and pre-clinical Bruker Albira Si combine SPECT, PET and CT into one scanner, enabling exciting opportunities for multi-radiotracer studies. At the same time, top-of-the-range multi-modality systems are expensive and *combining single-modality scans from different time-points and systems* can provide more cost-effective solutions and faster worldwide adaptation, which again demands the ongoing developments in spatial alignment.

While imaging research and software methods are both developing rapidly, the challenging opportunity for cross-modality synergistic methods remains open. We therefore need to consolidate our advances while also expanding our CCP PETMR network and software to exploit synergy in multi-modal, multi-contrast, multi-time point information for a greater range of applications.

In contrast to the majority of CCPs, a large part of our long-term impact is realised when the developed methods and software can be used by (pre)clinical researchers. However, *translation of advanced algorithms towards biomedical research* and (ultimately) clinical practice is essential but difficult [Coo06]. Incorporating advanced reconstruction software into processing pipelines for biomedical research needs effort on both networking activities and software, ideal for a CCP. We are therefore seeking additional funding from the Medical Research Council (MRC) to enable use of advanced methods and our software in (pre)clinical research, i.e. bridge the first Cooksey gap towards translation. Envisaged benefits are:

- *Increased statistical power* in (pre)clinical research studies, thereby allowing either detection of smaller effect sizes or reductions in the number of subjects and associated costs. This can be achieved by our software framework in different ways: i) use of advanced reconstruction methods; ii) for multi-centre studies, the use of standardised image reconstruction and software facilitates harmonisation, enabling a higher quality baseline across all centres.
- *Increased reproducibility* of results in (pre)clinical research studies, by providing access to comprehensive processing pipelines, from raw data right through to study outcomes.

Vision

In summary, there is great potential to increase our CCP's impact in the UK and beyond by i) consolidating current advances, ii) expanding into other imaging modalities, iii) serving not only clinical imaging needs, but now also preclinical imaging needs, bringing the benefits of a network of imaging experts and a unified software platform to the wider arena of biomedical imaging, and iv) translating the software towards use in large (pre)clinical research studies. The vision is to *establish a network and software to exploit synergy between multiple datasets for image reconstruction* in biomedical imaging**.** The network will connect two mutually-beneficial and overlapping communities: researchers in image reconstruction who develop advanced algorithms and software, and biomedical researchers who benefit from the software as described above. In this proposal, we initially target the modalities of PET, SPECT and MR, with other modalities such as X-ray and proton CT to be addressed via collaboration with other networks (CCPi, OpenRTK, the PRaVDA consortium).

Aims and Work plan

The proposed CCP SyneRBI has the following aims, targeted towards enabling and accelerating research in biomedical (i.e. both preclinical and clinical) imaging:

- Networking and community:
  - Bringing together expertise: improve communication between researchers and initiatives to advance the understanding of multi-modal imaging data, algorithms and scope for synergy.
  - Training the next generation: target young researchers, from Masters, to PhDs and postdocs to develop the future leaders in the field.
- Expanding open source software (OSS) infrastructure: enable researchers to use a high-quality common framework for cross-modality algorithm development, concentrating on SPECT, PET and MR reconstruction, potentially using "side-information" from images from other time points and imaging modalities. The software will be powerful enough to handle real data, but simple enough to be used for training and fast prototyping.
- Translation towards biomedical research: create validated comprehensive pipelines for raw-data-to-end-result in clinical research studies, and train end-users in advanced synergistic image reconstruction methods to enable proof-of-concept studies.

These aims correspond to work-packages (WPs) and below we assign a lead (one of the CoIs or CoSeC staff) to manage each task, with listed support from others where substantial. The PI will oversee and contribute to all WPs.

WP1: Networking activities and Community Engagement

All meetings will rotate around the network or organised before/during/after major UK and international conferences (e.g. IEEE MIC, PSMR, ISMRM, MICCAI, British Chapter ISMRM, SNMMI), allowing for online attendance and presentation whenever possible. Additional communication will be via the website, mailing lists, a YouTube channel with videos of meetings, tutorials and seminars, and GitHub for software development. We will encourage ECRs to take leadership of meetings, with mentorship by one of the investigators.

WP1.1 Bringing together expertise [AJR with DA, ME, CoSeC]

- Workshops (~7 half-day events and 1 three-day event) with scientific presentations related to synergistic reconstruction, focusing on topics driven by the interests and requirements of the network, e.g. modality-specific topics such as attenuation correction for multi-time point data; cross-modality test objects ("phantoms"); machine learning and multi-modality reconstruction.
- Quarterly software developer meetings discussing practical aspects and implementation.
- Twice yearly focused software development "hackathons".
- Funded exchanges within the UK and international network (sponsoring travel and living expenses). Visitors will be asked to give webinars with online streaming.
- Interact with other groups and networks with overlapping interests, including organising joint meetings. Specific initiatives contacted include: CCPi, DPUK and PET-MR harmonisation project, the recently funded National Cancer Imaging Translational Accelerator (NCITA), SNM/ISMRM PET-MR group, OSIPI for MR perfusion, the AI Centre at KCL, UCL AI CS. International initiatives on open standards (ISMRMRD, EANM, SNM).

WP1.2: Training [AJR with JM, CoSeC]

Training activities related to image reconstruction topics and sustainable software development will be via dedicated meetings, including hackathons, integrated courses at international meetings, and talks at relevant events (including EPSRC Centres for Doctoral Training). Training to use and extend the software will be incorporated into existing general image reconstruction courses. Video tutorials will be produced to help with software installation and example usage. Part of the material used in the training sessions will be re-packaged as video material and made available online.

WP1.3: Dissemination and Outreach [ChT with ME, CoSeC]

Specific actions are described in the 'Pathways to Impact'.

WP2: Software development and deployment

WP2.1. Code maintenance, optimisation and HPC [CoSeC with ME]

- Fold-in software contributions. Code with incompatible licenses will be rejected or replaced.
- Optimise execution speed (e.g. GPU). Investigate inter-engine communication mechanisms.
- Contribute to OSS packages to enable/facilitate SIRF integration, improve code quality and robustness and help adding missing features.
- Extend SIRF: support for temporal aspects; include handling of SPECT data; attenuation correction from (multi-energy) CT images or MR.

WP2.2. Integration of/interfacing with Open Source Software packages [DA with ME, CoSeC]

We have begun to exploit within SIRF numerical methods developed in CCPi through their Core Imaging Library (CIL) library and we will strengthen this interface. We will provide guidelines and work towards API definition for external packages to interface to SIRF, with expressions of interest from: CASToR (PET and SPECT reconstruction), NiftyPET (GPU-based PET reconstruction), OpenRTK (SPECT and CT reconstruction), motion estimation and modelling software currently under development at UCL. We will interface SIRF with OSS software for Deep Learning (TensorFlow, NiftyNET) to exploit the benefits of new machine learning techniques for image reconstruction.

WP2.3 Implementation of promising algorithms in the literature [ME with AJR, CoSeC]

Next generation reconstruction algorithms include synergistic e.g. [Ehr15, Meh19] and/or machine learning solutions e.g. [Arr19]. We will implement state-of-the-art optimisation algorithms e.g. [Cha18, MR19] to enable the latest developments in this field. Emphasis will be laid on the synergy between SIRF and CIL so that these algorithms are shared across both platforms.

WP2.4 Testing on simulated and acquired data [CT with DA, JM, CoSeC]

In addition to the continuous integration tests for the software, it is essential to test the results on data from all supported systems. Our simulation framework [May19] will be used to construct a database of multi-modality data for anthropomorphic computational phantoms. Additional phantoms and liquids for MRI acquisitions will be provided by Leeds Test Objects and scanned with all imaging techniques (PET/MR, PET/CT, SPECT/MR, SPECT/CT and MR-only, including pre-clinical where available). Simulated and acquired data, sample reconstruction scripts and resulting images will be uploaded to Zenodo.

WP2.5 Software deployment [CoSeC with ME]

Different users have different needs for installation. This task will build on strong foundations in the SIRF SuperBuild. Specific items include: conda support, MATLAB installation packages (for specific versions of MATLAB and operating systems), Singularity containers for clusters, additional cloud computing deployment via Terraform.

WP3: Translation towards biomedical researchers

For the image reconstruction framework to be used by biomedical researchers, logistical barriers need to be addressed and evidence of utility needs to be provided to give confidence to researchers regarding the capabilities and benefit of novel algorithms. We will address the former through additional software development and training and the latter through validation activities.

WP3.1 Software development for translation [DA with ChT, CoSeC]

XNAT is OSS and widely used in imaging trials for data collection and instigation of automatic processing, which can be on distributed systems via VUIIS/DAX. UK initiatives such as DPUK and NCITA are building software infrastructure for large clinical studies based on these platforms. We will add functionality for handling and processing of raw acquired data with SIRF enabling start-to-end pipelines. We will run hackathons to link our CoSeC software engineers with the existing UCL software engineers (part funded by this proposal) and other members of the network to share experience of image reconstruction and XNAT between these teams. Specific tasks include:

- Software for testing of SIRF using existing quality assurance protocols.
- Development of example XNAT+DAX pipelines for processing of data acquired on different systems according to fixed protocols with selected reconstruction algorithms. These pipelines will be made robust, including checks of data on input and logging for auditing.

WP3.2 Validation [JM with DA, ChT, CoSeC]

We will provide data and methods from which the benefits and limits of novel reconstruction algorithms can be determined. Specifically, we will:

- Establish and make available to the network suitable standard phantom acquisition and data-analysis protocols. Phantoms will be made available to network partners free-of-charge (see Letter of Support from Leeds Test Objects).
- Extend the number of datasets which we plan to provide as part of WP2.4 to the network, including data sets for quality assurance phantoms and scanning of phantoms at multiple sites.
- Look to acquire access to patient data sets suitable for validation through collaborations (see DPUK MR-PET partnership grant and Sydney VITAL SPECT-PET data Letters of Support) and establish and make available suitable data analysis methods for validation.

WP3.3 Training of biomedical researchers [JM with AJR, ChT]

- In addition to WP1.2, training will be provided which is oriented towards biomedical researchers such as NHS clinical scientists, (pre)clinical researchers and clinical academics. This will focus both on scientific findings, such as the benefits and limits of synergistic reconstruction, and on the logistics and practicalities on executing novel reconstructions using SIRF.
- Building on WP3.2, provision of training on how to assess advantages, limitations and compare SIRF with other reconstruction software will be provided, leading to exemplar studies that show benefit. The grant will enable such studies with their execution out-of-scope for this proposal.

CoSeC Core support

We are asking for 2.0 FTE per annum spread between 1.7 FTE for programming, 0.1 for project management and 0.2 for administration. The administration 0.2 FTE will help web-site management (with Wiki), mailing lists, organisation of workshops and meetings. The main effort will be dedicated to software development including maintaining documentation and other support: training in sustainable software techniques, establishing and enforcing coding standards, ensuring OS and compiler independence, release management, installation support, deployment via virtual machines etc. Specific tasks are listed in the WPs above. FTE per annum on software development is: WP2.1: 0.6, WP2.2: 0.3, WP2.3: 0.2, WP2.5: 0.3, WP3.1: 0.3. See Justification of Resources (JoR) for reduced funding scenario.

National importance and alignment with EPSRC and MRC priorities

The UK has pioneered many innovations in biomedical imaging, from CT (Hounsfield) and MRI (Mansfield) through to the first simultaneous PET-MR (pre-clinical) at KCL and the first clinical SPECT-MR co-developed by UCL. Initiatives such as the DPUK help UK researchers advance medical research with imaging. Software has an increasingly important role in imaging with artificial intelligence (AI) set to revolutionise the field, and OSS enabling entry-to-market for innovators. This interdisciplinary CCP will enhance the UK cross-cutting research capabilities identified by the EPSRC Healthcare Technologies (HT) theme (*novel computational and mathematical sciences* and *imaging technologies*) as well as EPSRC ICT portfolio priorities (d*ata dnabled decision making* and c*ross-disciplinarity and co-creation*). Synergistic imaging addresses two of the HT Grand Challenges (*Developing Future Therapies* and *Optimising Treatment*) by enabling UK and international researchers to develop and advance methods and software that extract information from all available imaging datasets to enable studies with higher statistical power (reducing costs and simplifying logistics), ultimately enabling Precision Medicine in challenging diagnostic settings.

While CCP PETMR enabled *basic and applied* research, fitting the first few technology readiness levels (TRL) along the HT translational development pathway, CCP SyneRBI now proposes enabling researchers to continue the translational development (TRLs 3-4).

Management Structure

An Executive Committee (EC) composed of the PI (chair) and CoIs will be responsible for the running of the network and software activities. The EC will keep track of software licensing and will keep the network within budget. The EC will meet every six weeks (usually online). A Steering Panel (SP), chaired by the PI, will decide on network activities and software efforts. The SP will suggest and coordinate further application for funding. Membership of the SP will be reviewed every year by the EC. The SP will meet twice per year. Two External Advisors (EA) will provide a yearly check on the project and give independent advice. The EAs are highly renowned members of the international community. The EAs will also be able to contribute to workshops and meetings as appropriate. In case one of the EAs resigns, the SP will propose a replacement.

Targets and performance indicators

Numbers are quoted as *x+y*, with *y* related to WP3 (see "reduced funding scenario" in JoR)

	Mid-term (10/2022)	End of grant (3/2025)
Networking		
UK Userbase	• 80+10 UK members	• 150+30 UK members
International links	• 2 International Researcher visits • 25+10 International members • Participation in 2+0 international training courses	• 4+ International Researcher Visits • 50+20 International members • Participation in 4+1 international training courses
Workshops/training	• 100+0 different people attended	• 200+60 different people attended
Developer community	• 8+2 active contributors • 4+1 hackathons	• 15+4 active contributors • 8+2 hackathons
Example datasets	• 15+20 phantom data sets	• 30+40 phantom data sets
Outreach	• Lay-section on website including a 3 minute podcast / video • Participation at science fairs in Bath, Leeds, Manchester, London	• Updated lay-section on website • In collaboration with the Institute of Physics and Royal Society promote 4+2 podcasts/webinars
Software Dev/ment		
Available software (fully documented and tested)	• Extend SIRF to SPECT, handle side-information from multi-time-points, including registration • Integrate 2 more OSS "engines" • 5 additional advanced algorithms • Initial interface to machine learning tools [WP3] • Software for test data analysis • Initial pipelines for PET, MR data incorporated to XNAT+DAX	• Extend SIRF for 4D data with cross-modality information including motion & scans from different time-points and systems • Integrate 3 more OSS "engines" • 10 more advanced algorithms • Machine learning with SIRF [WP3] • Software for data analysis • Validated pipelines for SPECT, PET, MR data into XNAT+DAX
High Performance Computing	• Optimisation & multi-threading for most intensive calculations	• Extend optimisation (GPU) for intensive calculations, including external OSS "engines"
Deployment	• Coding & documentation, docker, Virtual machine (VM) & Azure • conda, .deb package for Linux	• Coding, documentation, docker, singularity, VM, Azure & AW • conda, Linux .deb package, brew for OSX, installer for Windows

References

[Arr19] Arridge *et al*, Acta Numer., vol. 28, pp. 1–174; [Cha18] Chambolle *et al*, SIAM J. Optim., vol. 28, no. 4, p. 2783; [Coo06] Cooksey, 2006, A review of UK Health funding; [Ell17] Ellis et al. 2017 *Phys. Med. Biol.* **62** 6963; [Ehr15] Ehrhardt *et al*, Inverse Probl., vol. 31, no. 1, p. 015001; [Hut19] Hutton *et al*, Br J Radiol. Jan; 2018 91:1081; [May19] Mayer *et al*, proc. ISMRM 2019; [Meh19] Mehranian *et al*, *Magn Res Med*, 81(3):2120-34; [MR19] Mehranian&Reader, *Oral, IEEE NSS/MIC*, 2019; [Ovt19] Ovtchinnikov et al, *Comp. Phys. Comm.* (provis. accepted); [Thi12] Thielemans et al, *Phys. Med.Biol.*, 57 (4).867.