IN CONFIDENCE

UKRI Infrastructure Advisory Committee (IAC)

Text for submission as a full infrastructure project

Name of project	National facility for ultra-high field (11.7T) human MRI scanning
Type of infrastructure project	Establishing new capability
Lead Council/ UKRI team	EPSRC
Partner Councils/ UKRI teams /external partner	MRC, Wellcome
Short description of the project [max 250 characters/ approx. 50 words – to be used in any summary docs or briefings for IAC and ExCO] *A national facility for ultra-high field (UHF) human MRI. This will allow the UK's MRI research community to realise the substantial benefits of UHF MRI and exploit the advanced capabilities of an 11.7T scanner in ground-breaking studies that address crucial questions in biomedical research.*	

Costs table (£m)	Year					Total
	21/22	22/23	23/24	24/25	25/26	
UKRI Infrastructure Fund requirement						
Equipment	9.31	1.23	9.61			20.15
Building		0.77	1.23			2.00
Recurrent Equipment	0.09	0.09	0.22	0.51	0.51	1.42
Recurrent Personnel (incl. FEC)	0.34	0.34	0.65	0.65	0.78	2.76
Total	**9.74**	**2.43**	**11.71**	**1.16**	**1.29**	**26.33**
Any other contributions from other partners or UKRI budgets. Enables understanding of full cost of activity as well as Infrastructure Fund's part in this.	[if relevant to project]					

Database tool allows teams to adjust table format as needed to reflect the **partners involved, duration, resource and capital** needs for each project. Option to enter costs as **point estimate or express as a range**.

Teams will also be asked about:

- **scalability of options** (Y/N and if Y what range),
- the % of the investment allocated to **contingency** (if any) and the basis for that contingency.

1. **Description of the project and what it will enable** • Research/ innovation aims and objectives • What research would this project enable? • Why this infrastructure is needed (research/ innovation need) • Who this is for - potential target user base and evidence of community/market demand. Comment on any intention to target new types of user community • What success would look like after 5-10 years • Any other background or history it will be useful for the IAC to be aware of including spend to date

Research/ innovation aims and objectives:

Our vision is to establish a national facility for ultra-high field (UHF) human magnetic resonance imaging (MRI) scanning, based around an 11.7T scanner. This will allow the UK's MRI research community to realise the substantial benefits of UHF MRI and to exploit the advanced capabilities of an 11.7T scanner in ground-breaking studies that address crucial questions in biomedical research.

Our objectives will be to deliver:

• Robust acquisition of functional MRI (fMRI) data at 500-µm isotropic resolution, facilitating the characterisation of the laminar and columnar architecture of the human brain over extended cortical regions, and allowing the direction of information flow to be evaluated by comparison of laminar signals.

• Anatomical images with sub-100 µm resolution, providing histological levels of detail for identification of changes in brain architecture and microstructure in neurodegenerative, neuroinflammatory and neurodevelopmental disorders.

• Improved measures of metabolism in the human body, transforming our ability to undertake non-invasive studies of human physiology, and providing new insights into human biology and the mechanisms of disease and therapy.

• New MRI technology, along with the image acquisition and processing methodology, needed to realise the full benefits of 11.7T in the brain and body, which will also yield considerable benefits for MRI at lower field strengths.

What research would this project enable?

Magnetic resonance imaging (MRI) and spectroscopy (MRS) provide powerful insights into the structure and function of the human body, enabling the study of anatomy, physiology and metabolism, dynamically and non-invasively, in health and disease. MRI and MRS underpin research programmes across the whole of biomedicine, from basic human biology and neuroscience to experimental medicine studies and clinical trials.

The UHF scanner project will help to maintain the UK at the forefront of this economically and societally important field of research. Increased signal at 11.7T will translate into much richer information content in structural and functional imaging in the human brain and body, producing a step change in the range of research questions which can be addressed non-invasively with MRI. The signal-to-noise-ratio (SNR) of brain images will more than double from 7T levels, and sensitivity to key MRI markers of tissue properties will also increase. This is particularly the case for sensitivity to myelin and iron, which are important markers of neurodegeneration, neuroinflammation and neurodevelopment. Higher field provides stronger BOLD (blood oxygenation level dependent) contrast that forms the basis of most functional MRI (fMRI) of the brain. BOLD contrast scales approximately linearly with field strength, leading to a near quadrupling of the BOLD contrast-to-noise ratio from 7 to 11.7T. This massive gain in sensitivity will allow brain activity to be probed in unprecedented detail, enabling reliable assessment of brain function at a mesoscopic level, bridging the gap between invasive electrophysiology and microscopy techniques, and standard neuroimaging. As is evident from pre-clinical work, UHF also offers great benefits for studies of metabolism in health and disease using NMR signals from ^{1}H and other nuclei. Gains in SNR for MR studies involving other nuclei (including, ^{2}H, ^{7}Li, ^{13}C, ^{17}O, ^{23}Na, ^{31}P and ^{129}Xe) are even greater than for ^{1}H and these benefits are amplified by the greater spectral dispersion at 11.7T. Moreover, the radio-frequency (RF) coil engineering for many of these low gyromagnetic ratio species is more favourable at the high resonant frequencies provided by operation at 11.7T. Increased spectral dispersion and slower longitudinal relaxation also improve the specificity and sensitivity of ^{1}H chemical exchange saturation transfer (CEST) measurements. These factors will produce a step change in metabolic mapping capability by reducing the acquisition time required for useful, spatially-resolved measurements to a participant-acceptable duration.

Why this infrastructure is needed (research/ innovation need)?

The development of MRI has followed a trajectory towards ever increasing magnetic field strength, driven by the need for the increased sensitivity and contrast offered by operating at high field. We now have more than 14 years' experience of 7T MR in the UK, and UK-based researchers have helped to establish the efficacy of 7T MRI. Through the UK7T Network, the UK's 7T sites have gained valuable experience of close collaboration on UHF MRI. Experience at 7T and recent technological advances, have led to considerable international excitement about the potential of UHF (> 7T) for human MRI. A small number of 9.4T scanners are producing impressive results, 10.5T and 11.7T scanners are poised to deliver and 14T scanners are being considered in Europe and China. This mirrors the situation that pertained just before MRI researchers successfully moved up in field to 3T, and later, 7T. For UHF to gain real traction, a concentrated national-level effort is now needed to realise its full benefits. We believe that a step change in performance can be rapidly delivered at 11.7T, enabling swift advances in applied biomedical imaging, while the considerably larger costs, risks and timescale involved in developing a 14T scanner, make this an aspirational goal for the future. The potential gains offered by 11.7T are prodigious, but considerable technical advances in engineering, physics and computer science are required to deliver them. The world-leading, closely-knit UK research community is well-placed to undertake the coherent programme of work required to develop and exploit 11.7T.

Who this is for - potential target user base and evidence of community/market demand.

Insights into brain structure and function will be of immediate benefit to researchers in basic and clinical neuroscience. New measures of metabolism and organ function from basic physiology to studies of disease will be of value across the biomedical community, including the life science and healthcare industries. Engineers, physicists and computer scientists will be engaged in the development of new UHF technology. The facility will thus enhance the research portfolios of EPSRC, MRC, BBSRC and Wellcome.

The drive to establish this facility has been stimulated by: (i) recent advances in the physics and engineering that underpin high-field MRI, (ii) growing understanding of the efficacy of 7T MRI, and (iii) ongoing work to establish UHF MRI capabilities in other countries (e.g. plans for a 14T MRI scanner in the Netherlands, and a concerted US effort to gain support for a 20T MRI scanner). An UHF MRI workshop (> 130 attendees) was held in Nottingham in January 2019 to promote community engagement in the development of an UHF facility. It brought together international pioneers of UHF MRI with potential developers and users of UHF MRI in the UK. Subsequent discussions with the Research Councils led to an invitation to submit a Community Statement of Need (CSoN). This statement was developed over a one-month period in May/June 2019, with input from ~90 researchers from 20 different organisations (University of Birmingham [Birm], University of Bristol [Bris], University of Cambridge [Cam], Cardiff University [Car], University of Edinburgh [Ed], University of Glasgow [Gla], GSK, Imperial College [Imp], The Institute of Cancer Research [ICR], KCL, University of Leeds [Leeds], University of Liverpool [Liv], University of Manchester [Man], Newcastle University [New], University of Nottingham [Nott], University of Oxford [Oxf], University of Sheffield [Sheff], University of Sussex [Suss], Tesla Engineering Ltd and UCL). The CSoN received very positive reviews from six international referees. A new version of the CSoN which was revised to address the reviewers' comments, was submitted in December 2019 and is attached to this paper as an appendix, along with the reviews of the original submission.

Examples of science that will be enabled by the new facility, as detailed in the CSoN, include (with participating sites noted):

Developing new technology and methodology for MRI: The 11.7T facility will advance the state-of-the-art in high field engineering through new innovations and perform key safety studies. It will (i) establish national capability for UHF RF coil design and fabrication (*Bris, Gla, Nott, Sheff*); (ii) optimise parallel transmit (pTx) techniques, essential for imaging the head and body at UHF (*Cam, Car, KCL, Nott, Sheff, UCL*); (iii) develop motion and field monitoring methods for prospective and retrospective correction of effects of movement in images and spectra (*Cam, Car, Nott, UCL*); (iv) investigate the effects of microstructure on contrast mechanisms (*Bris, Cam, Car, Nott, Oxf, UCL*); (v) use very high quality 11.7T data sets in conjunction with machine learning to augment data acquired at lower field via quality transfer (*Nott, Oxf, UCL*); (vi) develop 2D-MRS approaches for improved *in vivo* measurement of brain metabolites (*KCL, Man, Nott*); (vi) provide RF safety data and model RF interactions with the human body at 500MHz (11.7T) (*Nott, KCL*).

Assessment of brain function at a mesoscopic level: The near quadrupling of the BOLD contrast-to-noise ratio from 7 to 11.7T, along with the enhanced sensitivity of other functional measures, will allow the (i) establishment of laminar-specific fMRI as a tool for investigating information flow in the cortex during task execution and for evaluating mesoscale connectivity, underpinned by improved understanding of laminar haemodynamics (*Birm, Cam, Gla, Nott, Oxf, Suss, UCL*); (ii) probing for evidence of columnar organisation in cortical areas outside the visual cortex (*Cam, Birm, Gla, Man, Nott, Oxf, Suss, UCL*); (iii) investigation of changes in responses across laminae in neurodegenerative disease, specifically testing the hypothesis that Parkinson's and Huntington's disease affect deep layers of the cortex early in the disease course while Alzheimer's disease involves more superficial layers: combined with anatomical images this will provide mechanistic insights at the earliest stage of these diseases, when therapeutic intervention would provide greatest benefit (*Cam, Nott, UCL*).

Anatomical images with histological detail: The signal-to-noise-ratio (SNR) of brain images will more than double from 7T levels, and sensitivity to key MRI markers of tissue properties, such as myelin and iron will increase. This will allow the (i) detection and characterisation of small microbleeds and their links to disease mechanisms including neuroinflammation, vasculopathy, trauma and neurodegeneration (*Birm, Cam, Liv, Man, Nott, UCL*); (ii) elucidation of neurodevelopmental disorders, including focal cortical dysplasia, and the earliest stages of neurodegeneration that are poorly seen at lower fields, using increased sensitivity to investigate the role of immune cells in neurodegeneration based on differential iron accumulation in microglia and macrophages (*Birm, Cam, Car, Ed, GSK, Imp, Liv, Man, Nott, Suss, UCL*); (iii) characterisation of sub-cortical structure; this will allow investigation of sub-nuclear pathology, improved targeting of therapeutic deep-brain stimulation and characterisation of nuclei in the medulla which have vital homeostatic functions (*Birm, Cam, Nott, UCL*); (iv) measurement of key structures (and physiological processes, such as vascularity and hypoxia), that underpin therapeutic success and clinical outcome in cancer, exploiting new contrast and theranostic agents (*Birm, ICR, Man, UCL*); (v) harmonising anatomical contrast at 11.7T to conventional histology through linked post-mortem MRI and microscopy (*Oxf*).

Improved measures of organ metabolism: Gains in SNR of MR measurements from other nuclei (e.g. ^{2}H, ^{13}C, ^{19}F, ^{31}P, ^{23}Na,^{129}Xe) and greater spectral dispersion at 11.7T will provide a step change in metabolic mapping capability by reducing the acquisition time required for useful spatially-resolved measurements. This will allow the (i) use of ^{13}C-MRS and MRI to quantify endogenous metabolites and study the metabolism of exogenous ^{13}C-labelled metabolites (*New, Nott*); (ii) application of ^{19}F MRI to tracking of perfluorocarbon-labelled cells in regenerative medicine studies and monitoring of neuroinflammation (*Cam, Gla, New*); (iii) use of ^{31}P measurements to probe the mitochondrial redox potential through the NAD/NADH couple (resolvable in UHF preclinical systems, but so far challenging at 7T in humans), with particular application to psychiatric studies and investigation of cardiac disease (*Cam, KCL, Leeds, New, Oxf, Sheff, Suss*); (iv) use of ^{23}Na MRI to quantify cell volume fraction for evaluating atrophy in neurodegeneration, monitor therapy in cancer and investigate mechanisms of functional failure in multiple sclerosis (*Birm, ICR, Imp, Nott, Suss, UCL*); (v) exploitation of increased spectral dispersion and sensitivity in 2-hydroxyglutarate measurements as a marker for isocitrate dehydrogenase mutation in tumours, particularly for assessing tumour heterogeneity (*Ed, Gla, ICR, Liv*); (vi) use of CEST and deuterium metabolic imaging in measurements of normal and disturbed metabolism (*Cam, Car, GSK, Man, Nott, UCL*); (vii) development of UHF methods for dissolved-phase ^{129}Xe imaging of the brain and kidneys that allow assessment of membrane permeability and tissue perfusion (*Sheff, Nott*).

What success would look like after 5-10 years

We will develop an operational 11.7T scanner in 30 months, for utilization in parallel programmes of further technical development and neuroscience exploitation. Five years post-award the facility is projected to have more than 100 active users (less than 30% being from the host site and more than 10% being international); more than 50% of the running costs will be raised on a full cost recovery basis via access charges raised from UK grant funding or from industrial or international funding sources. The rest of the costs will be covered by core funding that will provide an essential pump-priming resource at the critical exploratory stage in the establishment of this new technology. This core funding will also be used to support the development of the more advanced features of the system, with the goal of achieving full exploitation of parallel transmit and multi-nuclear capabilities in the brain and body. In ten years, a successful facility will have produced at least 100 high-impact papers, contributed to the training of more than 200 doctoral students, and more than 100 researchers. The facility will have participated in hosting more than 100 international visitors. By this stage the running costs would be fully covered by access charges.

2. Has the potential for excellent research and innovation been independently verified?

A Community Statement of Need (CSoN) for the *National facility for ultra-high field (11.7T) human MRI scanning* was submitted in June 2019 and independently reviewed. This statement, which follows the format developed by EPSRC for evaluation of bids for National Research Facilities, received very positive reviews from six international referees. A new version of the CSoN which was revised to address the reviewers' comments, was submitted in December 2019 and is attached to this paper as an appendix, along with the reviews of the original submission.

3. What are the strategic drivers of this project?

[This might include Council Delivery Plan or industrial sector strategy; UK business need; a UKRI 2025 goal; international diplomatic driver or international leadership considerations; government policy need; local or place related factor; legal or regulatory obligations; strategic partnership opportunities.

Aim is to highlight the clear line of sight to specific drivers rather than general statements referencing 'contributions to 2.4%' or 'underpinning the industrial strategy' which are relevant to all projects.

Strategic Drivers

The plan to develop a *National facility for UHF human MRI scanning* that will hugely enhance the range of anatomical, functional and metabolic features that can be detected *in vivo* using magnetic resonance is well aligned to relevant components of the Research Councils' 2019 Delivery Plans. In particular, the development and exploitation of an 11.7T human scanner will contribute to EPSRC's Objective 1 on *Delivering economic impact and social prosperity*, (specifically, its *Healthy nation: Transforming healthcare,* Research and innovation priority) through provision of improved understanding of disease and treatment, and will also contribute to its Objectives 2 and 3 on *Realising the potential of engineering and physical sciences research*, by calling on the unique UK expertise in MR physics and hardware engineering in developing the UHF scanner, producing new technology and methodology which will also impact upon MRI at lower field strengths, and on *Enabling the UK engineering and physical sciences landscape to deliver*, by provision of a unique platform internationally for cutting-edge, biomedical imaging research. The proposed facility would also help to realise several of the long-term ambitions set out in MRC's Research and Innovation Priority in *Discovery Science* - particularly in strengthening *our knowledge of the human brain, including neural and glia cell biology, neuronal circuits and brain function, bridging the knowledge gap between the 'micro' (molecules and cells) and the 'macro' (behaviour in society)* and in improving *our understanding of how the immune system interacts with tissues during homeostasis and ageing, and in diseases ranging from infections to cancer, degenerative and chronic* *inflammatory disorders*, as well as providing a platform for research studies that address four of MRC's seven Health Focus Themes (*Precision Medicine, Multi-morbidities, Advanced Therapies* and *Mental Health*).

The UK holds a world-leading position in medical imaging research, with an exceptional track record of success stretching back to the invention of CT and MRI. The proposed project will help to maintain the UK at the forefront of this economically and societally important field of research. The researchers who contributed to the development of the CSoN are directly supported (as PIs) by >£50M of current research funding from UKRI and Wellcome, with additional funding from a range of other sources (including EU, NIHR, Alzheimer's Research UK, BHF, CRUK, Cystic Fibrosis Foundation, Michael J. Fox Foundation, MND Association, Parkinson's UK, UK MS Society, Weston Brain Institute, Spinal Research and Versus Arthritis), indicating the broad range of research that will rapidly benefit from the proposed national facility.

The development of a flagship UHF facility in the UK will stimulate the MRI industry in the UK. A recent report commissioned by STFC to analyse the impact of this industry on the UK economy suggested that it made *a value-added contribution to UK GDP worth £111 million in 2010, once the industry's multiplier impacts were considered,* and *supported around 2,200 UK jobs*. *Between 2011 and 2015, the industry and its multiplier impacts* were *expected to contribute between £587 and £685 million to UK GDP in total*.

4. What are the potential economic and/ or social benefits of the project?

Comment or expand on direct and potential indirect benefits where this has not already been covered in the overview. These could be economic, social, environmental, health, public service or policy improvements. These might accrue from the construction/ project implementation phase or be as a consequence of the outputs over the longer term.

If available flag references to any evaluations or existing evidence of impact, particularly if proposal is related to upgrades where it is reasonable to expect some assessment of previous activity will have been done. There is no expectation of economic modelling and analysis at this stage but please include any relevant data if this has been undertaken.

Potential economic and/ or social benefits of the project

As a platform for world-leading biomedical studies, the facility will have significant societal impact via provision of better understanding of human brain function and anatomy in health and disease, along with new insight into normal and disturbed metabolism and physiology throughout the human body. It will allow the implementation of studies which can currently only be performed in animal models, so helping to bridge the translational gap between preclinical and clinical studies. The facility will also support pharma R&D by producing a flow of sensitive and specific biomarkers of disease that allow early interrogation of pharmacological responses, so providing improved understanding of drug mechanisms of action. UK research communities which will benefit from the facility include: neuroscientists, who will exploit the increased spatial specificity and sensitivity at 11.7T in interrogating brain structure and function; clinicians and life scientists in academia and industry, who will use UHF MR to investigate disease mechanisms and therapies in the brain and body, particularly supporting experimental medicine and early target validation/efficacy studies at Phase 1-2b in patients with chronic disease; physicists and engineers, who will develop and apply new techniques and hardware for UHF MR; computer scientists and mathematicians, who will exploit the previously unattainable spatial resolution and information content of 11.7T data.

The cutting-edge developments in MR technology, required to realise the benefits of the elevated field strength, will open up new opportunities for commercialisation, and, in many cases, these developments will also be applicable at 7T and lower field strength, so providing far-reaching benefits for research and clinical studies. Enhancing the UK's capability in RF hardware development will have significant enabling impact for MR research in the UK, potentially stimulating the development of new SME's, as has occurred in Germany and the Netherlands. Significant impact could also arise through use of ultra-high-resolution 11.7T data to augment lower-field measurements via machine learning. The improved understanding of microstructure, anatomy and physiology that 11.7T MRI/S will provide will also underpin improved acquisition, analysis and interpretation of lower field data.

UK industry has played a leading role in the development and supply of magnets for MRI, and until recently had supplied all magnets for human MRI scanners operating above 7T. This document has been developed in discussion with Tesla Engineering Ltd, who have provided information on magnet characteristics. Tesla employs 150 staff in the UK who are engaged in the development of UHF MR, and the associated supply chain underpins a significant number of specialist engineering jobs in the UK. The development of an 11.7T magnet for use in a national facility would provide a significant stimulus to the magnet industry. The availability of a showcase 11.7T scanning system will provide a significant stimulus to the international market for MRI, boosting an area of industrial strength in the UK.

A national facility for UHF (11.7T) MRI is needed to maintain the UK's position at the international forefront of research in the development and application of biomedical MR. It will form a focus for international collaboration, with direct links to the leading international sites who also aspire to develop an UHF MRI scanning capability, as well as drawing in collaborators without access to UHF technology in their own countries. The facility will attract and retain world-leading scientists in the UK – this would include clinicians, physicists, engineers, clinical scientists and neuroscientists. It will also provide a focus for training of researchers in the engineering, physics and application of UHF MRI, benefiting the wider MRI research community. The contributors to this bid collectively have an extensive network of multi-disciplinary collaborations within academia, industry and charities, which will be leveraged to expand the user-base of the facility.

This national facility will provide a focus for training of researchers in the engineering, physics and application of UHF MRI, and since this training will focus on the foremost technical challenges in MRI, it will also benefit the wider MRI research community, including the UK7T Network and a number of imaging-focused doctoral training programmes. The new facility should form the focus for a distributed centre for doctoral training focusing on UHF MR acquisition and analysis methods, with students from participating sites coming together for regular training, summer schools, and to share their research experience. This training platform will generate cohesion across the user-base of the facility and help to develop the future leaders of biomedical imaging in the UK.

5. How is this a step change in infrastructure capability and how does this fit into the existing infrastructure landscape?

Include:

- how this was covered in the Infrastructure Roadmap report (which focused on step changes) –include the reference to the relevant sector and theme - no requirement to repeat any text from this report.
- what similar or other capability already exists in the landscape if any (UK or internationally where UK users' access) and explain how this would complement, replace or expand capacity.
- If a project is scalable comment on how the proposed scale might impact on ability to create a step change

Infrastructure Roadmap report

An ultra-high field 11.7T MRI scanner facility will provide the UK research community with a step change in capability to apply structural and functional imaging to study of the human brain and body in health and disease (as described in the CSoN). The need for the development of an UHF scanning facility was highlighted in the UKRI report on *The UK's research and innovation infrastructure: opportunities to grow our capability* in the context of both the *Biological sciences, health and food sector* (*Theme 4: Human phenotyping (at depth and scale))* and the *Physical sciences and engineering sector (Theme 4: Technologies to improve health and treatment)*. The UK7T Network, which underpins this application, forms the basis of a Case Study of *Connecting capability at a national scale* that is included in *Chapter 10: Evolving and connecting the landscape* of the same report.

International Landscape

Today, around 20% of the approximately 3,000 new scanner installations per annum operate at 3T, and with the recent CE approval and FDA clearance of the Siemens 7T Terra scanner for examinations of the head and extremities, sales of 7T scanners have accelerated and the range of applications of 7T MRI is rapidly growing. At present, there are more than seventy 7T scanners worldwide. In the UK, seven 7T scanners are operational (in order of installation - Nottingham, Oxford, Cardiff, Cambridge, Glasgow, London Queen Square UCL, and London St Thomas' KCL). There are a small number of individual sites internationally operating MRI scanners above 7T. There are three operational human 9.4T scanners in Europe (MPI for Biological Cybernetics, Tübingen, Germany; Maastricht University, Netherlands) and the US (University of Illinois, Chicago), and one is under development in China (Institute of Biophysics, CAS, Beijing). The University of Minnesota operates a 10.5T scanner and three 11.7T scanners are expected to become operational in the next two years (NIH, USA; Neurospin, Saclay, France; Gachon Medical University, Korea). Several national-level initiatives for developing UHF scanners are planned. In the US, a concerted effort to gain funding for a 14T scanner is underway, with the ultimate aim of producing a 20T scanner for the human brain. The Netherlands and Germany have both formed national consortia to develop 14T MRI systems (neither yet funded). We are also aware of at least two groups in China (Shenzhen Institutes of Advanced Technology & Peking University) who have received funding to begin the development of human 14T projects.

A field strength of 11.7 T offers a significant increase over 7T in sensitivity for anatomical and functional MRI, as well as providing major benefits for spectroscopic measurements of metabolism and kinetics, based on ^{1}H and a range of other nuclei. An 11.7T scanner can be built around a magnet that uses the well-established NbTi wire technology that is employed in lower field scanners (although requiring pumping to achieve a wire temperature of ~2K) and could be constructed in less than two years. By harnessing the collective effort of the UK MRI research community, we can therefore develop a powerful and versatile UHF scanner, enabling swift advances in applied biomedical imaging that can be exploited in studies of the brain and body within three-years of the start of funding. In contrast, a 14T scanner, although providing additional gains in sensitivity, would require more complex NbSn wire technology, which is yet to be incorporated in human MRI scanners. The cost, lead time and risk of failure involved in developing a 14T scanner are all significantly higher, and the time required to develop a working system would be greater than 5-years.

6. Feasibility and delivery:

Comment on:

- Stage of development of this project [with reference to guidance and following approach from Infra roadmap] i.e. if this is at an early stage the IAC need to know as less information will understandably be available – this may be converted to a drop-down selection for ease.
- Overview of delivery approach and why this was chosen (e.g. this is a new facility, hosted by a particular institution, a new partnership) including proposed project governance, project management approach and SRO (if known)
- If relevant describe what options analysis has been undertaken to decide on this approach [IAC can ask to see this]
- Where the infrastructure is based around a technology please indicate why this technological approach was chosen over alternatives and if the technical feasibility has been externally assessed. If this is to be completed briefly comment on plan to do this. [if a detailed analysis exists reference here and IAC can ask to see this]
- Key partners (if relevant) and whether this involvement has been secured or is hoped for [IAC may ask for evidence that partner involvement has been secured such as a letter of support from co-funders]
- Top risks and challenges to delivery (excluding lack of funding)
- Major delivery dependencies and assumptions

Stage of development

This project is at Stage 3 of development (*The concept for the infrastructure requirement is clear and ready either to progress to implementation or to conduct a pilot, scoping or design study which will refine delivery or technical options and allow for more informed decisions on whether or not to proceed further*) as defined in the recent UKRI Infrastructure Roadmap report.

Overview of delivery approach

The CSoN was prepared on the basis that the *National facility for UHF human MRI scanning* would be hosted by a single academic institution with well-established research infrastructure for biomedical imaging and operated in partnership with other participating institutions. It is expected that there would be a competitive process through which sites could bid to host the facility. The project to establish the facility would be managed by the host institution calling on its central services (estates, finance, procurement, legal, contracts etc) in a process co-ordinated by the Facility Manager.

Technological Approach

The scanner will utilise an 11.7T magnet with a large enough bore (830mm) to accommodate gradient and RF coils that allow measurements to be made in the body, as well as in the brain. A gradient coil (610mm inner diameter) capable of producing gradient strength/slew rate of at least $80mTm^{-1}/200Tm^{-1}s^{-1}$ will be incorporated, and an insert head gradient coil to provide significantly higher gradient performance for neuroimaging studies (e.g. for high-resolution tractography) will also be developed. A minimum of 16 ^{1}H transmitter (Tx) channels (2kW per channel) will be used to achieve homogeneous excitation at 500MHz by exploiting parallel transmit (pTx) methods. At least 128 receiver (Rx) channels will be available, ideally configurable across different resonance frequencies, to facilitate a range of multi-nuclear studies. 32kW of reconfigurable RF power would be available for X-nuclei studies. The system would initially be supplied with 16Tx/32Rx ^{1}H RF head and body array coils, along with combined $^{2}H/^{1}H$, $^{23}Na/^{1}H$ and $^{13}C/^{1}H$ RF head coils, as well as quadrature T-R switches for bespoke coil interfacing. Additional multi-nuclear RF coils would subsequently be built or purchased, to support a wider range of studies. An optical camera for monitoring head motion and a field camera for measuring spatiotemporal variation of the fields in the magnet will be incorporated. Capability for monitoring physiological information synchronised to scan acquisition will be provided, as well as standard peripheral devices for fMRI studies (video, audio and vibrotactile stimulus presentation systems and response boxes).

A detailed specification of the equipment required is given in the response to Q7 of the CSoN, along with the arguments underpinning the selection of system characteristics. An update on major system components is provided below, along with an assessment of the main risks and challenges to delivery. Different elements of the system (magnet, shielding, spectrometer and associated hardware) would be sourced from different suppliers, but the integrated system supplier would take responsibility for system integration.

Magnet and shielding £8.05M: The 11.7 tesla, 830mm bore specification for the magnet is carefully chosen, based on known technology and a price-performance which gives maximum return and value. A slightly lower cost magnet could be specified by compromising the useable volume, but this would restrict studies to the brain only, while multiple researchers are interested in exploiting the advantage of UHF for studies in the body. A higher field strength was not chosen because of the long lead-time for magnet delivery and untested nature of the required technology. With at least two potential suppliers of the magnet, we are confident that an 11.7T/830 mm bore magnet can be delivered within two years of order. The main risks to cost and supply are: (i) currency fluctuations, since superconducting wire and other materials are generally sourced internationally; (ii) increases in the price of liquid helium due to market volatility in the face of the current limited supply. As reflected in the above price, the cost of the magnet and shielding has increased by £0.4M since June 2019 due to increases in helium and wire costs. Several new sources of helium are expected to enter the market in 2020 and 2021, easing the supply issue.

Integrated system £12.1M: With three major MRI scanner providers capable of undertaking the supply of spectrometer and associated hardware, it is likely that a competitive tendering process will result in the leveraging of gains in terms of in-kind contributions and/or cost price reduction. The suppliers all have experience of at least 7T operating field and would be capable of supplying and integrating the system. The multi-nuclear probes will generally operate at lower frequencies than current 7T ^{1}H RF technology (300 MHz) so this aspect is low risk. The top risk element is the supply of 500 MHz RF probe technology, which would be mitigated by developing a significant UK research programme in RF coil development.

Building £2.0M: An indicative cost has been included based on a design study at the University of Nottingham, but this cost would vary with location and host institution.

System Total Recurrent over 5 years £1.420M: These figures are projected from indications from suppliers. Again, for the 5 years of the funded period these would be negotiated as part of the overall system supply contract.

Personnel Costs over 5 years £2.76M: Enabling the UK research community to realise the full benefits of the UHF scanner, will require the facility to provide expert staff support. Various roles will be phased in over 5 years. A Facility Manager is needed to manage the specification and ordering of the system, and its subsequent installation, testing, and operation. Two postdoctoral research assistants (PDRAs) are needed to develop, test and manage RF coil hardware over the 5-year period. It is expected that these PDRAs will form part of a wider, cross-institutional collaborative effort in RF coil development. Once the system is installed, three PDRAs will work with users to develop and optimise sequences for functional imaging, anatomical imaging and spectroscopy. Research radiographer support will be needed in Year 5 to run studies based on established sequences.

7. Can you confirm this will be open to users outside of those directly involved in the project (i.e. the host institution and funding partners)?

The defining nature of the Fund is a presumption of open access beyond the institution in receipt of funds otherwise funds will not be allocated. Bids are asked to confirm this is the case and briefly state how they will do this (user access strategy or model).

For full implementation cases bids required to say what action will be taken to develop the user base, promote and support access widely in target communities (this might include raising awareness through to active training of new users or dedicated support staff).

Advisory Committee (and endorsing Councils or expert groups) will be asked to consider if the proposal is considering a wide enough user base and if plans are likely to encourage this but particular models of access will not be required. No common assumptions will be made about proportions of users from outside the institution or from business/overseas etc.

Vision and support for access

Our vision is to establish an *open access* national facility which will bring together the UK research community to realise the benefits of UHF MRI.

We aim to develop an 11.7T MRI scanner that can be exploited by researchers in a range of studies, particularly for experimental medicine and neuroscience. Through a collective national effort, we will develop a state-of-the-art scanner that is optimised for operation at UHF, integrating recent enabling technical developments into the design, including open architecture, high-density RF receive arrays, pTx capability, and motion and field monitoring. The specification of the scanner will be developed with the community through a robust procurement process, preceded by an initial design phase. Elements of this design will facilitate the future development of more versatile scanners operating at lower field and help to shape the future development of even higher field scanners (14 and 20T).

In addition to the space required for housing the scanner and its control/equipment rooms, the facility will require patient-friendly reception and waiting areas, as well as rooms for behavioural and neurophysiological testing. It would be expected that the national facility would be associated with an existing imaging centre with experience in managing high-end medical imaging scanners, and in close proximity to a university hospital. This would mean that the necessary ancillary facilities and support structures (including those required for data storage and transfer, quality assurance, clinical research support and governance, and potentially for RF coil development and testing) could build upon existing structures and systems. The new facility would also require office space for hosting visiting researchers over both, medium- (e.g. 3 months to implement and test a new sequence or RF coil) and short-term visits (e.g. a oneday visit to scan multiple subjects). A key role of the host site will also be to enable patient studies, through provision of appropriate local facilities and links to local clinical collaborators with access to a diverse range of patient groups. The network of NIHR Biomedical Research Centres (and key clinical academic centres in the devolved nations) offers a natural engagement mechanism for this activity, particularly in supporting experimental medicine and clinical trial research. The bid to establish the UHF scanning facility has received the support of the NIHR Imaging Steering Group.

Operational Model and Managing Access

Several models for funding the operational costs of the facility during its early phase of operation will be considered in discussion with UKRI: a multi-institutional programme grant alongside an infrastructure award could fund the development of the system, with this activity utilising a significant fraction of the time on the scanner; or this development could be proportionally funded by multiple academic institutions (in conjunction with funders) in return for involvement in the development programme and early access to the scanner.

In the longer term, we envisage that recurrent costs would be covered by access fees paid through grant funding (in line with most UK research scanning facilities). Based on the current cost of 7T scanning (~£700 per hour), a charge of £1,000 per hour is realistic for an 11.7T scanner. At this rate, 16 hours of fully funded scanning per week over 48 weeks per year would cover the estimated primary operating costs of the facility (maintenance contracts, facility manager and radiographer). This would leave significant capacity on the scanner for continued development work, maintenance and pump-priming activity.

Key committees will be established to ensure facility access and operation is managed effectively.

A *Steering Committee*, comprised of representatives from multiple institutions (including clinicians, neuroscientists and physicists), industry and funding bodies, will set and oversee the parameters of the facility's operation. This committee would agree the process for allocation of time on the scanner during the early phase of system development and then with a modified approach in the later phase of full cost recovery, during which subsidised access for pilot work will still be provided.

An *Operational Committee,* composed of active developers/users of the facility, would meet frequently to manage the facility's operation. A joint *Safety Committee* would also be established with the UK7T Network and the committees would be informed by input from an *International Advisory Board*, including representation from international sites with experience of human scanning above 7T.

8. Impact on environmental sustainability

Environmental sustainability will be a major consideration at every stage in the development and operation of the UHF scanning facility.

We will work with the manufacturers to limit the materials and energy usage of the UHF scanner. This will involve minimising the use of liquid helium (a finite resource) in cooling the magnet and maximally recovering helium gas that boils off during cool down and normal operation – efficient use of cryocoolers in magnet cool down and consideration of the feasibility of shipping a 'cold' magnet from the site of manufacture will be key in this regard. Cryocoolers and other scanner systems generate a significant amount of heat that is generally dissipated via water cooling systems in modern scanners. We will aim to recover waste heat for use in the building operation. If successful, this innovative approach could be exploited in a wider range of MRI scanner installations. We will use suppliers exploiting renewable energy sources where locally available.

We will consider the Life Cycle Carbon Footprint (LCCF) of the building that will be used to house the facility (for example exploring the relative LCCF of refurbishing an existing building versus construction of a new building).

We will ensure that the *National facility for UHF human MRI scanning* is sited at a location with good, sustainable transport links, and in operating the facility we will develop ways of working that allow users to minimise travel to the facility, including supported remote operation of the scanner, which could also considerably enhance user engagement.