Appendix 1: Breakout Reports from the BioImagingUK Strategy Meeting

These reports summarise discussions and conclusions from the individual BioImagingUK Strategy Meeting Breakout groups. The named authors have contributed to the final document and these texts have been used to build the Strategy Meeting Summary Report.

I. Electron Microscopy

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Through several rounds of consultation and incorporation of interest from different EM communities (e.g. structural biology and cell biology EM), the following plan has been developed to fulfil the needs of the overall UK Biomedical EM community for the period up to 2020. This EM community includes all kinds of Biomedical EM, ranging from (pre-) clinical to basic research, incorporating animal and plant research.

Electron Microscopy is able to provide a unique set of data, e.g. providing a direct ultrastructural reference space for structures or molecules of interest. Most EM techniques, however, require a high degree of specialisation. Although this is discussed in more detail in other sections of this document, we would like to emphasise that, because of the specialised nature of EM, it is extremely important to provide clear and stimulating career pathways both for the technical support staff as well as for the “EM scientists”. This includes stable positions, career perspectives, and continued training.

The major principle on which this proposal is based, is that in order to ensure a sustainable Biomedical Electron Microscopy infrastructure, it is essential to maintain the solid foundation of “basic” EM facilities spread over the UK. The vast majority (probably over 90%) of the excellent UK electron microscopy that is published within peer-reviewed journals is performed in these local university and research EM facilities. This broad-based EM community is where the majority of future “EM scientists” (from technicians to principal investigators) get their first experience of electron microscopy and is also the natural starting point for the numerous preliminary experiments that in some cases will lead to more complex scientific questions possibly requiring more sophisticated instrumentation and/or expertise not available locally. However, we also recognise that in order to fulfill the demand for ever-more specialised, exotic and (ultimately) expensive techniques there is a need for some centralisation of specialist facilities. We envision a 3-tiered structure based upon the complexity of the technique, the need for expert support, and the (running) costs of the instruments.

University and Research Institute EM facilities:

Existing local facilities will serve the vast majority of EM projects for Biomedical research as they are based on routine applications (SEM / TEM) but are able to provide unique data sets. These types of facilities are critical to provide the groundwork for more complex analysis and therefore the provision, maintenance and replacement of “lower-end” instruments *must* be protected. We emphasise that the National Facilities and Centres of Excellence proposed below should not preclude other facilities from performing or acquiring such high-end technologies, rather, they act as a resource to researchers that cannot afford or do not have access to those technologies and expertise at their home institute. It is also important to highlight that technology and instrumentation are developing rapidly and equipment that is seen as highly specialised or very costly today, may in a few years time, become commonly available in the local facilities. Such developments need to be monitored and evaluated on a regular basis.

Local Facilities will not be able to provide all the techniques, equipment, and know-how to cover the wide range of EM analysis techniques. This may, for instance, depend on the nature of the technique or associated costs. To allow ALL UK biomedical researchers

access to such (“higher-end”) technology, a network of more specialised Centres of Excellence and 1 or 2 National Facilities are required.

Centres of Excellence:

Centres of Excellence will provide access to cutting-edge technology that does not necessarily require extremely expensive equipment but rather very skilled staff that are able to perform and support the execution, interpretation, and analysis of experiments. These types of technologies are not used on a day-to-day basis in biomedical research but do require dedicated equipment. A bundling of resources in a limited number of centres across the UK would provide a very cost-effective model. Such centres should also provide training for new researchers in the field and in that way allow the dissemination of the methodology to the wider UK EM community. Funding for this type of centre should be at a national level with application, for instance, as a distributed network to the Science and Technology Facilities Council (STFC).

1. Correlative Light and Electron Microscopy (CLEM) - distributed network across the UK, providing expertise, training, and access. These types of centre need to be associated with both down- and up-stream technologies (e.g. different types of light microscopy, culture facilities, and sample preparation methods).

2. Cellular Electron Tomography - Room temperature Electron Tomography is a very valuable research technique that not always requires the highest resolution instruments but does need dedicated staff, especially for the data analysis.

3. Analysis Electron Microscopy – Increasingly, the techniques of what traditionally were considered material science EM are also being applied to biomedical questions. Technologies such as EDX, STEM, SIMS, GIF, and EELS have already shown their use but they are not applied widely, mainly because of the unfamiliarity with the technology.

4. Cryo FEG SEM – High resolution biological SEM is best performed on samples that are in their native state, i.e. frozen rather than chemically fixed. There are only a limited number of such systems available in the UK because handling and imaging these samples is not easy. Opening such instruments to the wider community as Centres of Excellence will create completely new opportunities for research.

5. Other technologies that should also be considered are: Cryo preparation and Focussed Ion Beam technology in general.

National Facilities:

National Facilities will provide access to newly developed technology that is so expensive that few systems can be acquired nationally. Currently we foresee the need for 2 (or 1 integrated) large-scale institute(s) that would provide instruments and expert support. Funding for these resources should be at a national level and access charges should be subsidised (similar to synchrotron at Diamond).

1. High-Resolution TEM – focusing on 300kV microscopes for cryo EM and electron tomography. This will be the prime resource for structural biology (single particle EM and cryo tomography) and will include 3D cellular EM. A proposal has already been submitted to construct a national facility at Diamond, which is currently under discussion with the funding bodies (Wellcome).

2. Volume SEM – automated physical sectioning and imaging within the SEM chamber over hundreds of microns^3 at nanometre resolution. This technology is suited to acquiring lower resolution, but high volume information from cells and tissues. Instruments such as Focused Ion Beam SEM (FIB/SEM) and Serial Block Face SEM (SBF/SEM or 3View) could run in a 24/7 acquisition mode, producing large datasets. This could be run largely as a remote service, and would require expertise in sample processing, data acquisition, image analysis and large-scale data handling. This is a fast-developing field with new, expensive instruments coming to market in quick succession. This Facility is under discussion and it must be emphasised that rather than going for the highest resolution, the aim is to provide volume information within the tissue reference space.

The aim of extending and formalising the transfer of key skills and knowledge from the Centers of Excellence and National Facilities to the wider UK EM community will be further enhanced by the provision of a specialist EM equipment "loan pool". This will be facilitated by close ties to equipment manufacturers to allow evaluation and (where appropriate) adoption of specialist and newly emerging technologies able to advance UK biological sciences. The equipment will be loaned with training and ongoing support to academic groups [loan periods will be adjusted to reflect any installation and training demands associated with individual technologies up to a maximum period of 12 months (e.g., initial 6 with 6 month extension)].

This will allow UK researchers access to highly specialised, novel or emerging technologies that cannot be readily evaluated due to their high capital cost. Manufacturers will provide demonstrations but these can be unhelpful in establishing the value of a technology in answering fundamental biological questions. They are conducted over a limited time period, and sometimes seem to be designed to disguise instrument limitations and promote sales. The provision of extended loans, with technical support and training will allow the world class biological research groups located in the UK to critically evaluate new technologies capable of advancing their biological research with the technical support of experts in the field. It is envisaged that loan of the technology will lead to:

a) Sufficient pilot data for the group to justify seeking funding for essential/ proven core equipment,

b) The totality of a focused research agenda leading to publication

c) Identification of technical limitations which either require further refinement by the manufacturer or which preclude the technology from effectively contributing to challenging the biological question.

This initiative will significantly reduce the waste of time and money caused by equipment being purchased too early in its development cycle or purchased without sufficient pre-training or evaluation to allow the research group to fully capitalise on the investment and minimise the initial, scientifically unproductive training period. Additionally it will allow early adoption of emerging or refined methodologies by UK scientists without the risks outlined above or the lag associated with the process of capital equipment purchase. This relationship should also aid the equipment manufacturers (many of who are UK-SME's) as it will help them with instrument and software design, refinement and development. It is envisaged that the sort of equipment available within such a "loan pool" would include (but not be limited to); cryo-rods, dual axis rods, plunge freezing equipment, high pressure freezers, EM detectors (ED/ WD), SEM-cryostages, direct detection digital cameras etc. Data from loans will be collated to support the general Bio-imaging community in the UK, providing a resource of technical data assessing the capabilities (and deficiencies) of a

wide range of highly specialist technologies that many researchers might be considering for their projects but don't have the time, capital or expertise to evaluate.

II. Light Microscopy

Breakout Leads: Peter O'Toole (York), Dave Stephens (Bristol), Rafael Carazo-Salas (Cambridge)

Visualisation of sub-cellular structures and even single molecules is absolutely essential in biological and biomedical research for our understanding of complex biological morphologies and functions. Thus, light microscopy has developed into one of the most widely used imaging modality in the tool kit of bioscientists. Light microscopy is limited by the diffraction of light, defining a relatively low spatial resolution of 200 – 300 nm laterally and 500 – 700 nm in the axial direction. Although transmission electron microscopy (TEM) provides unsurpassed ultra-resolution down to the nm range, it comes with a range of significant technical limitations in terms of molecular labelling, complex sample preparation and the lack of live cell imaging.

However, recent developments in light microscopy have successfully circumnavigated the diffraction-limited resolution barrier, closing the resolution gap between conventional fluorescence microscopy and EM by offering a whole range of novel approaches allowing super-resolution fluorescence microscopy (SuRFM) and improving the spatial resolution of up to a magnitude. Currently, these systems are not yet standardised, and thus require significant initial investment and support for personnel trained to maximise the utility and use of these systems.

In the breakout discussions, the overall goal was to define mechanisms that:

- Enable technologies across UK science that have not previously been available, thus maximizing return in the form of high impact science and avoiding poor utilization.
- Give more users open access to state of the art technologies, where percentage use would be low.

Technology and resources that coordination and strategic delivery will help ensure are

- Ultra high end, expensive equipment (e.g., highly specialized, technically demanding instrumentation, >500k): we saw this as a 'national facility', hard to replicate, requiring specialized expertise to run and maintain, best to centralize for niche expertise. Critical to also have peripheral equipment for upstream/downstream experiments (tissue culture, cell sorting, genomic analysis, etc.).

- Emerging technologies (super-resolution microscopy, high-throughput/high-content screening, FLIM, FCS and other specialist technologies): best delivered through, 'Centres of Excellence', that provide external access for proof of concept and knowledge transfer. These nodes would interact to form a distributed network, where appropriate, integrated with a local core facility. As above, they would need upstream/downstream peripheral equipment and resources.

- An on-line "virtual community", as a repository of user tips/methodologies/etc as well as how/where to access specialised equipment.

All of the above require a critical mass of biological expertise, staff resources and a strategy for sustainable management (staff resources, maintenance contracts, running costs), which applies to all microscopy facilities from the fundamental to the high end.

Funding

Significant instrumentation, staff resource and management running costs that supports a critical mass of biological expertise, staff resources and a strategy for sustainable management (staff resources, maintenance contracts, running costs).

- UK funding bodies: 50% matching funding schemes are untenable; capital costs have been reasonable; any capital investment needs to be matched with good expertise resources and running costs; simple staff resource initiatives to enable the capital investments!
- EU: UK funded nodes could be put forward for EuroBioImaging
- Interaction with vendors: Nodes should engage with vendors to enable rapid and wide exploitation by other research groups.

Impact

By developing the above, this would:

- Enable technologies across UK science that have not previously been available, thus maximizing return in the form of high impact science and avoiding poor utilization.
- Give more users open access to state of the art technologies, where percentage use would be low.

III. Preclinical Imaging

Breakout Leads: Luc Bidaut (Dundee), Erik Sahai (LRI), Kurt Anderson (Beatson), Mark Lythgoe (UCL)

Preclinical imaging encompasses a wide variety of disease models and imaging modalities including MRI, PET, SPECT, CT, ultra-sound, and optical instances. The promise of preclinical imaging lies in the ability to interrogate in-vivo physiological disease models at the molecular level, thereby accelerating the development and translation to the human of new approaches and therapies. The main quandaries of preclinical imaging include the relatively high cost of infrastructure, the nurturing of expert multi-disciplinary teams, and an intimate dependence on animal work with its many restrictions. The funding challenge therefore extends well beyond the cost of acquiring, maintaining and updating sophisticated imaging systems, as the development and support of the necessary associated infrastructure (e.g., the specialist multi-disciplinary staff, the animal facilities, the biochemistry and radiochemistry for probe development, and the physical housing of these in functional proximity) also need to be accounted for. Accordingly, the broader challenge lies in the coordination of multiple bodies to ensure that the appropriate level of funding is reached in support of the whole.

Expert staff are critically important for pre-clinical imaging, yet their importance is consistently undervalued by funding agencies and by the current metrics of academic institutions. PhD level imaging staff lack appropriate career paths and funding mechanisms to support them, particularly in universities if they do not progress to PI status. Maintaining a stable team is a critical challenge in a multi-disciplinary environment with multiple and often unfit recognition metrics.

Finally, there is the overarching restraint of providing value for research money by serving a wide range of users, especially early career researchers or others aiming to establish novel scientific collaborations and/or research programs. This requires balancing development and sustainability of imaging technology with its application through provision of open access.

Main Action Points:

1. Develop coordinated multi-disciplinary funding strategies for equipment, staff, probe development, and biological services.

2. Develop career paths and funding mechanisms to support core expert staff.

3. Streamline, rationalise and standardise regulatory procedures to increase national competitiveness and facilitate access.

4. Devise new sustainable business models to facilitate user access and promote novel research.

If these issues are not addressed there are a number of predictable outcomes. The first is that the UK will simply not achieve the critical mass necessary to compete internationally at the forefront of preclinical research, which is an essential component of most basic and clinical research. A second outcome is that there will be a significant loss of momentum - and of any returns expected from previous commitments - for a substantial portion of active and/or promising research that requires preclinical imaging to develop further. A third likely outcome is that academics and expert PhD level staff alike will flee the UK for countries where intertwined PI and non-PI careers are better supported, such as those countries which actively adopt the strategies of EuroBioImaging. A final consequence is that the pharmaceutical industry will turn elsewhere for preclinical drug studies, further exacerbating the exodus of big pharma and associated funding from the UK.

The UK preclinical imaging community is united in the desire to act coherently and co-operatively for preventing the aforementioned outcomes and moving ahead. We are confident that, with the cohesive support of UK funding agencies, significant strides can be accomplished towards bringing optimally distributed preclinical imaging critical mass to the UK, which is a necessary means to ensuring the UK's international standing on all prospects that intrinsically depend on it.

IV. Medical Imaging

Breakout Leads: Dave Hawkes (UCL), Vicky Goh (Kings), Julia Schnabel (Oxford), Jo Hajnal (Kings), Daniel Rueckert (Imperial), Paul French (Imperial)

Initial Discussion:

About 20 people attended the medical imaging break-out. We started with about 30 minutes of open ended, free ranging discussion. Main points:

1. **Open Access:** Many of us are in effect providing “open access” to facilities already, albeit with charges for use of imaging equipment. Many research imaging facilities are used for (indeed depend on) external investigator (own institution and external to institution) research, though time has to be paid for and most centres charge running costs plus capital depreciation and so costs can appear high. Most facilities that allow external access for research have a management committee to allocate time and a steering committee to ensure scientific quality and to balance the research portfolio according to sponsors’ and institutional priorities. Inevitably there will be a bias towards own institution activity and an emphasis on activity that aligns with the research interests of the Principal Investigators linked to the facility (i.e. those that raised the funds for it). Involvement of facility PIs in project planning, fund raising and publication (e.g. if appropriate via co-authorship on published output) is usually expected. Most facilities are over committed and so rationing of time and prioritisation is inevitable.

Open source software tools for image analysis are an important component of “open access” to facilities and many of us contribute to such repositories. ITK, VTK, MITK, NifTK and the

combined CTK were all mentioned as being important in the medical imaging research domain.

There is growing demand for “open data” and the collation and curation of large open imaging datasets available to imaging research community. Examples mentioned include the ADNI and ACRIN datasets in the US. The UK could have a much more dominant role in this activity and the appropriate national institutions should facilitate this (but often doesn’t). Issues of patient privacy and ethical approvals need to be addressed and regulatory requirements streamlined to make this more efficient and effective. Better national coordination with major initiatives such as BioBank and other local data collections could provide a significant opportunity for the UK. This is also discussed below.

2. **Clinical Trials vs Methods Research:** There was a clear distinction articulated by the participants between sharing facilities for running clinical trials, effectively as an imaging CRO (either as a hospital, university or commercial entity) vs sharing facilities for doing methods research. There are a number of models for the former, including commercial organisations and not-for profit centres (e.g. the Bristol Imaging Centre www.bristol.ac.uk/cricbristol or Imanova www.imanova.co.uk) as well as hospitals and universities but it is the latter (sharing facilities for methods research) which was relevant to our discussions.

3. **Geographic Distribution of Expensive Facilities:** The optimal geographic distribution of facilities nationally is not straightforward and there was some resistance to the idea of having a strict top-down policy for this distribution. Coordination is certainly needed but expensive facilities are usually the result of local efforts by the imaging and clinical researchers involved with the support of specific host institutions. Having said that the preferred options for many is imaging research centres as regional centres. Despite comments at the meeting, patients do in special circumstances travel to where there are specific facilities, and in rare cases this may even include travelling abroad.

4. **Disconnect between methods research and clinical research**: Academic clinical research and clinical trials work can be very isolated from good imaging methods expertise so some way of accessing such expertise would be very helpful.

A Medical Imaging Research Strategy:

We then had about 30 minutes of more focussed discussion about a medical imaging research strategy and open access “nodes” of specific excellence.

Generally a more coordinated approach was seen as a very good thing with some provisos:

In favour:

1. Enabling 1 – 4 above

2. Opportunity to coordinate research activity – especially research requiring lots of infrastructure (e.g. big data, multi-modal imaging, linking with pre-clinical, complex data processing, etc etc)

3. Improved efficiency thru’ reduced duplication of effort/expertise

4. Standardisation of acquisition and processing – we all want this but a coordinated approach with imaging researchers at an early stage just makes this easier to do.

5. Related to this is “open” data. Funders, institutions and research leaders should encourage open data even for small scale studies. Once benefit becomes apparent to the data creators (more citations of own methods research, faster achievement of patient numbers – specially in rare disorders, higher impact publications) and some of the regulatory

and technical barriers encountered setting this up are overcome, then as happened with the open source software model, the concept will “snowball”. There remains too strong a sense of proprietorial ownership of publicly or charitably funded data collections with key PIs anxious not to publish lest their competitors publish a finding from the data that they missed. This might partly be overcome by enforcement of open access by funders (e.g. Wellcome with publications) and partly by stronger recognition of the scientific input of the data collectors via co-authorship in publications.

6. Not discussed but added later. Should we encourage “open” data acquisition, i.e. the intriguing idea of an “open” MRI scanner – where all pulse sequences etc are open – needs standardisation of hardware which may be difficult, and would change completely the business model for research MRI (and other scanner) facilities. This paradigm might also work for inherently cheaper technology such as ultrasound.

7. Leverage new money thru’ industry buy-in/shared facilities – but need to make sure something is in it for both sides, perhaps an innovative approach to IP could be promoted – with larger incentives for inventors – while avoiding the pitfalls of IP sharing.

8. Establish a sustainable and stable infrastructure that is not dependent on short term funding success.

9. Effective, sustained, critical mass for lobbying to improve and streamline regulatory, ethical and clinical governance landscape – for example, aim for all patients in Academic Health Science Centres having a blanket “opt-out” presumed consent for use of anonymised data.

Cons (although all these would could be addressed by the “node” infrastructure concept and become pros):

1. Getting the balance right between providing a paid for “service” and “active research collaboration” with the recognition that the latter deserves.

2. Getting academic credit for the large effort required to establish a node/facility

3. Scarce, high quality technical/engineering expertise and very poor career path for these people.

4. Relatively poor track record of centralised facilities – technology goes rapidly out of date, overly bureaucratic and inefficient. This probably applies more to the clinical image trial as service model rather than the node as centre of innovative scientific excellence.

The Medical Image Research Node:

We then developed the concept of the Medical Imaging Research Node.

1. A relatively small number of centres around “big imaging” research – e.g. 7T, 9.4T whole body facilities, PET + cylclotron + radio chemistry/ligands, multi-modal imaging facilities, other expensive and exotic technologies - all developed in a strategic and coordinated way.

2. A larger number of specialised “nodes” each innovating in a specific area, and each acquiring a critical mass of science/engineering/ICT/life sciences/clinical research expertise. These would supply open access for collaborating researchers to further the technology, feed-back novel applications and prepare it for roll-out to clinical research and ultimately clinical practice.

3. The virtual node for big data sharing/storing all relevant info with imaging, developing open source ICT solutions.

There was remarkable consensus for these 3 conclusions and interest in seeing how these resonate with the other groupings (em/optica/pre-clinical).

Finally we refer to the recent EPSRC strategy document on medical imaging research (http://www.epsrc.ac.uk/SiteCollectionDocuments/Publications/reports/EPSRCMRCMedicalImagingTechnologiesReport.pdf) which covered many of these issues.

V. Training

Breakout Lead: Alex Laude (Newcastle)

As the world of biomedical imaging continues to move forward, the demand for scientists who understand imaging in all its complex ramifications and who can help design and produce the imaging technologies of the future will continue to increase. In particular, there will be a need for more scientists who can transcend the disciplinary boundaries and who can combine biological and medical insight and knowledge with the development and refinement of imaging technologies.

A new breed of imaging scientists, with greater insight into the biological and medical fields, would help ensure that future imaging technologies and methodologies are more effective at improving human life through scientific discovery and clinical application. Equally, by exposing biologists and medical students to biomedical imaging courses (encompassing probe design, underlying physics and signal processing aspects of the technologies) will help them to realise the true potential of these technologies and result in more effective usage. A basic understanding of cellular, molecular and systems biology will improve collaborations between imaging technologists (physicists, mathematicians and engineers) and life science users (biologists, clinicians and non-clinicians), and, most importantly, provide both with insight into the technology requirements for the foreseeable future.

Training programmes are an effective way of building capacity in a given area. They would stimulate increased use, and demand for, new and existing technologies. Training will help to make imaging technologies more accessible to other disciplines and open up new avenues of investigation, with new requirements, challenges and directions being put forward by users. In addition to academic benefits, effective training programmes can augment industrial involvement in the biomedical imaging community and enhance knowledge transfer between the two sectors.

New student training programmes for imaging research at multiple levels will be important for the continued growth in this field and to ensure that emerging technologies are used and applied to their full potential. Imaging training offered at both undergraduate, postgraduate and continuing professional development levels, with short courses ranging from basic, advanced, to highly specialised, would be beneficial to the biomedical imaging community as a whole.

Post-graduate training

Implementing MSc/PhD training programmes with some sort of imaging component, will not only help produce the multidisciplinary imaging scientists of tomorrow, but will help build links between supervising academics from different disciplines. If structured effectively, new postgraduate student training programmes will help enhance current multidisciplinary collaborations and boost the application of imaging technologies. This may be achieved on a number of levels and will depend on the technology and level of student involvement. In imaging-heavy research projects, students would have at least two supervisors for their PhD

project (e.g. a technologist and a biologist) and work in two or more different research environments.

The successful 1+3 year MRes+PhD training programme format could be adopted providing time for specialised training across the different intellectual cultures demanded by imaging-based science. Such a programme could begin with a one-year full-time MRes, to encompass taught lecture modules on elementary and advanced aspects of biomedicine, imaging techniques and applications. Students will therefore be exposed to different scientific cultures and ensure that they experience technological development as well as application.

Ongoing training schemes

There should be a mechanism to train existing researchers and technical staff wishing to get more involved with imaging at whatever point of their career and importantly, when it is required. These persons would fall outside the above formal training structures and depending on their background, may have diverse requirements. The need for training in many cases may be immediate for example, in preparation for an imaging-based project. Many institutions offer imaging workshops / training opportunities but due to economic and time constraints, these are infrequent and may not deliver the required content. Better promotion through a centralized training portal of imaging-based workshops on offer throughout the UK would allow those requiring training that is not available in their host institution, to choose an event with the required content and at the required time. This portal may run along side existing RMS-related workshops and training events or through the BioImaging UK Wiki.

New approaches to teaching and learning

With the rise of new types of media for teaching and learning (e.g., MIT's OpenCourseware, http://ocw.mit.edu), the appearance of on-line video journals (JoVE, http://www.jove.com/) on-line and even University-branded YouTube channels, the opportunity for using new types of media as a training reference can now be seriously proposed. Indeed reference sites of microscopy are now routinely used (ADD EXAMPLES?!?). These types of resources can be accessed by students from the UK and beyond, and can establish the UK as a hub for knowledge and usage of bioimaging.

And if we don't ….

A populous of insufficiently trained imaging scientists can have a number of direct and indirect consequences.

A poor appreciation of the technology resulting from a lack of or ineffective training will no doubt manifest itself in improperly followed procedures, errors in judgment, misinterpretation of data and improper equipment usage and maintenance. There will be obvious detrimental impacts in terms of the quality and validity of data collected as well as equipment upkeep.

A cohort of poorly trained and less rounded imaging scientists and technologists will be unable to fully appreciate, apply and develop current and advanced technologies. This will have knock on effects in terms of scientific impact, development and funding of cutting-edge imaging-based science in the UK. The imaging scientists of tomorrow are the future of biomedical imaging to put it simply, if these scientists are not trained effectively then the caliber of imaging-based science in the UK will suffer.

VI. Probe Development

Breakout Leads: Tony Gee (Kings), Nick Long (Imperial)

The Challenges

Probe and biomarker design and development is crucial for the future of biomedical imaging across the scales and imaging modalities. Arguably, probes have become the rate-determining step for further development of several imaging modalities. Novel probes are certainly required (particularly 'smart' and multi-modal), but alongside these there needs to be better use made of existing biomarkers and contrast agents.

There sometimes appears to be a "disconnect" between the makers and users of probes. For example, there is a perception that probe development is sometimes driven by the developers' interests - chemists do not want to be used as a 'service' for users where there is no academic challenge. Do the users know where to go or who to ask for a probe – and do probe makers listen to requests? More interaction and dialogue needs to take place across the probe development communities and between developers and users.

There is perhaps redundancy in probe development across different imaging platforms e.g. a ligand/probe developed for one modality could be used in a different modality/setting. More effective transfer of knowledge/data across modalities would clearly be beneficial. There are many databases on probes but they are often specialised and there is scope for a universal database of probes. The same probe can work in different ways under different conditions and so specific application information needs to be shared.

Where probe development or synthesis is routine there could be a better balance between commercial provision and synthesis by staff. Open access to imaging facilities would increase burden of probe preparation (e.g. radiochemistry) and of labelling strategies (e.g. transfection of FP etc). Other hurdles to probe development and application are MHRA, GMP and legislation. Training of staff at an early stage would help here.

Actions/Solutions

Funding/incentives are needed to help facilitate interactions across the communities – motivating *both probe makers and users*. Funding should be truly translational across Research Councils, to overcome issues e.g. such as perceived insufficient novelty of probe chemistry (for EPSRC) or biomedical impact of probes (for BBSRC/MRC). Funding by e.g. BBSRC 'Tools and Resources', small scale grants could support proof of concept of probe development.

There could be a Doctoral Training Centre in the development and application of probes - involving supervisors of complementary expertise, e.g. from biological/clinical application to synthetic chemistry. Address "disconnect" by more multidisciplinary training at PhD and PDRA level. More 'rounded' chemists could be trained that understand translation/application of the probes that they make. UK needs to ensure a pipeline of good people at every level, i.e. student, PDRA, senior scientists, expert technician, academic.

Need broad-ranging teams (involving expertise across the disciplines) to have flexibility in probe development. Going from high-risk adventurous probes to standard/routine probes that already have a clinical application – Centre/Programme grants could facilitate this. National Nodes for probe development chemistry could be created at centres of excellence (perhaps alongside high level, expensive imaging equipment and infrastructure) whereby a 'nodal timeshare' is created where in return for some funding. Standard probes could be synthesised, made available and distributed for ca. 20% of the researchers time.

Unfortunately some medical (radiochemical) probes need to be made 'fresh' due to short half-lives and this provision has to be more of a 'service' in its nature – thus chemistry to serve nuclear imaging is an issue. It is suggested that certain labs could receive core funding to synthesise and distribute certain known radiochemical probes for the community.

UK national meetings, such as last year's successful meeting on Probe and Biomarkers for Biomedical Imaging held at the RSC, could be held regularly – and sharing best practice for probe design and application across the modalities. To help users identify suitable partners

to develop probes, there could also be funding for a central networking resource i.e. creating a 'dating agency' for users/developers. Create links/expertise/knowledge base across Europe, and have synergies across platforms and modalities from medical through to biological imaging. Some ligands/probes could be universal. Researchers within a particular imaging modality tend to work and remain together as a community, whereas a bigger pool of researchers, from across the imaging modalities but interested in probe design and their utilisation, who regularly meet and discuss issues would be hugely beneficial.

Results of Inaction

The field will continue to develop in a fragmented and piece-meal fashion.

Major advances in probe design will still occur but cutting-edge developments in producing new materials and new synthetic or labelling methodologies will be slowed down.

The development and utilisation of some imaging modalities will slow (sometimes dramatically) without the advances in probe design and improvements in areas such as toxicity, solubility, bio-compatibiity, non-specific binding and most importantly, targeting of the imaging agents.

Diagnosis and patient treatment will suffer and have negative socio- and economic impact across the healthcare sector.

VII. Careers

Breakout Leads: Martin Spitaler (Imperial College London, Raffaella Carzaniga (Cancer Research UK, Peter March (University of Manchester), Amanda Wilson (Imperial College London, Paul French (Imperial College London)

Expert imaging staff who have the experience and skills to provide access to high level instrumentation, including imaging technology, are increasingly critical to the research mission – and this need is particularly increasing in the life sciences. For imaging based science, this includes experts in hardware and software. Such people can sustain and develop technical expertise in facilities and research institutions and are in demand globally. In line with its international competitors, the UK needs to recognise that such staff are an essential part of any investment in advanced technology. Long-term career (>5 years) development is essential to attract and retain highly qualified staff in a global market. Many excellent scientists would prefer a career working hands-on with technology rather than the regular PI track, and such a career track would provide more opportunities for good scientists to contribute to the research mission. It would also catalyse better interaction between the academic and commercial world of technical development, e.g. helping to translate novel tools to biomedical discoveries and technical academic developments to viable commercial solutions.It should thus be presented as a career option at postdoctoral level.

The main needs with respect to careers of imaging (and similar) staff are:

- a new job description and career track ('Imaging technologist', 'scientific officer' or similar) – that is distinct from a PI research scientist but also distinct from a technician. Imaging technologists should be PhD level scientists with a long-term career structure that makes this career choice viable and attractive. This exists to some extent in research institutes but is particularly needed in universities. Some universities and

institutions already have such job descriptions that could be used as a model, e.g. CRUK or the University of Bristol.
- this job description has to be wide enough to cover all staff involved in making advanced technology accessible for research scientists, e.g. application of novel technologies for new biological / medical projects, participation in technological development (hardware, probes, analysis tools, ...)
- funding bodies and institutions must both agree on responsibilities towards such staff; for example, universities could provide the jobs and guarantee long-term commitment, while funding bodies contribute indirectly through user charges in research grants
- long-term job perspectives do not mean uncoupling job security from performance, but performance criteria need to be adjusted to the specific role (recognising that such staff aim to facilitate rather than lead research and may not compete with academics in terms of personal recognition, e.g. via publications.
- this “new” career track does not need to be exclusive of 'academic research', and lateral mobility between career tracks could be useful.
- development of instruments and techniques by such staff (including that which does not directly lead to publications) should be encouraged and be regarded as a normal part of the role.
- the new career option needs dedicated models for training and continuing professional development, taking into account the highly inter-disciplinary role (biological and medical research, physics, computing, mathematics, chemistry, management)

VIII. Access

Breakout Lead: Dave Stewart (STFC)

Requirements for providing access to advanced imaging capabilities:

- State-of-the-art equipment
- Multidisciplinary support team
- Training for users – providing advice and help with probes and sample preparation
- Specialist data analysis techniques and data storage/handling

Issues:

- Facility needs to be flexibility and have routes for increased capacity and/or capability to meet extra demand and to be able to upgrade capabilities to provide the very latest techniques.
- There must be an appropriate balance between resource and capital investment. Capital investment requires significantly more resource funding to enable best use.
- Access models for facility - free at point of access or user charges, or somewhere between the two (e.g. a user charge but some subsidy to make access feasible).
- Facility access provision should not be at the expense of innovation/technique development. Instrument developers should work closely with facility providers but may not necessarily be directly involved in facility provision
- The UK community needs to express its opinions about how we prioritise investment in the large number of potential facilities.

IX. Software and Data

Breakout Leads: Richard Baldock (MRC Edinburgh), Sebastien Ourselin (UCL)

SOFTWARE:

1/ Clear agreement that it should be Open Source - ideally fully open for any use to encourage uptake and allowing commercial "added value". As far as possible there should be a common software framework

2/ Need a central mechanism to capture software and encourage/enforce standards and perhaps to maintain software tools that have been submitted and converted to the standard. This could reduce costs for data analysis – particularly for early career staff. Should we consider NAMIC as a potential model for software?

3/ Data visualization is a critical issue, particularly for multidimensional data. Community could perhaps look at the US NAMIC example to support visualization and image processing software

4/ Need software as libraries for developers to develop their own image analysis tools as well as turn-key systems that can be used by domain experts rather than software developers.

5/ Validation of data sets: community should establish ground truth data and setting of challenges; share best practice and adopt data and software standards to facilitate cross-validation.

6/ Training is critical and some nationally-coordinated approach would be useful and would also help drive standardization of software tools and data formats.

DATA

1/ Medical and imaging data very different with different "drivers" in terms of research

- archiving requirements certainly differ in term of permissions and approvals
- perhaps analyse via use-cases to establish common requirements

2/ Archiving mechanism with distributed curation and mechanisms to query and access data

- requires standards for exchange formats, metadata, annotation and especially linked data for studies.
- needs setting of minimum standards, defining/adopting ontologies and mechanisms for access

3/ Perhaps look at LONI as a model for archiving of subject specific data (in this case brain images) to deliver an open database with mechanism for query. A national centre could provide hosting but more likely expertise and support to enable groups to develop their own.

4/ Perhaps integrate the types of standards for image data used in the medical field to basic biological data?

5/ Data sharing is mandated and important

- need to share Images + Meta-Data + Provenance + Studies
- need standard ontology
- need algorithm validation
- need capability for statistical analysis of large cohorts