

APPENDIX 2

Problems encountered by the award holders during projects

The problems encountered by the award holders during the projects are detailed in this appendix. These have been categorised under different headings as listed below:

➤ **Patient recruitment**

- Problems recruiting healthy volunteers
- Number of patients within institution was low so the study had to be extended to another hospital
- Problems in obtaining cohort for follow-up studies
- Recruitment rate was slower than expected
- A large proportion had already agreed to participate in other studies
- Repeat attendance such as for follow up scans, was a deterrent
- Lack of compensation for travelling expenses affected participation
- Several patients underwent the initial study but then did not subsequently undergo surgery for medical or personal reasons
- Patients were unwell after chemo or withdrew from the study
- Recruitment of patients with glioblastoma who were clinically well enough to undergo adjuvant chemoradiotherapy was challenging. There was a period when several patients who had undergone surgery for a glioblastoma, developed post-operative or clinical complications and were unable to commence chemoradiotherapy. It was the intention that MR Spectroscopy (MRS) would be used to assess for metabolic changes within the invasive margin as a further measure of tumour progression. MRS was acquired at the initial imaging points for two of the recruited participants and preliminary analysis was performed. Towards the end of the treatment regime, there were some instances when these could not be performed due to the clinical deterioration of the participants. At these times, only the standard clinical sequences could be performed.
- Most patients with peripheral nerve injuries had secondary psychiatric and substance abuse issues. This led to a very poor uptake into the project.
- Although patients are being identified, the waiting list for the patients continues to be long; up to 18 weeks. This means that there is a delay before recruitment of specific patient groups can occur on the day of procedure.
- Recruitment of suspected intrauterine growth restriction (IUGR) foetuses was very disappointing and overall not sufficient.
- As all patient travel costs were not met by the NIHR Biomedical Research Units (BRUs), time was also spent on funding application to Radiology Department at hospital.

➤ **Resources not available**

- Lack of expertise on 4D flow sequences meant lack of adequate support and guidance
- Personnel required to provide stellate ganglion blockade moved away
- It was not possible to accommodate MRI scan times at very short notice
- The available magnetically-enabled guide wires were not as stiff as conventional guide wires to cross most of the coronary lesions encountered in this population
- The magnetic navigation lab was not readily available for angioplasty procedures
- Competition on time to use imaging equipment

- Lack of availability of scanner
- Upgrade of the 3T MRI system within hospital
- Availability of R&D research nurse support
- The bariatric surgery service was moved to a different site in the same trust
- Difference in techniques between different centres
- Some patients did not undergo all the necessary pre and post surgery lung function evaluations due to a combination of machine failure and logistical errors.
- Imaging software was not available; team members had little experience of image manipulation tools.

➤ **Methodological problems**

- During the study, a competing technology to the one being studied, became available which disrupted the progress of the project
- Co-registration between modalities and between imaging and histology
- Pathological specimens at recurrence were rarer than expected
- International shortage of helium for experiments
- Equipment frequently unusable due to the nature of prototype technology
- Low arthroscopy conversion rate
- It was the intention that MR Spectroscopy (MRS) would be used to assess metabolic changes within the invasive margin as a further measure of tumour progression. MRS was acquired at the initial imaging points for two of the recruited participants and preliminary analysis was performed. Titanium screws and postsurgical material present in the craniotomy site overlying the site of tumour resection resulted in artefact which prevented analysis of the voxels adjacent to the surgery site. As the recruited participants to this study all had surgery, MRS acquisition was discontinued at this point
- The image quality of intravoxel incoherent motion (IVIM) MRI sequence required for this project was limited by low signal-to-noise ratio. This resulted in poor reproducibility of the various parameters extracted from this technique,
- As the more optimised technique was being developed, there was need for more intensive Medical Physics input as the scanner settings were systematically adjusted beyond the vendor presets.
- In order to preserve integrity of the data in the prospective part of the study, only patients whose studies were performed with similar technical settings to the final iteration were included in the analyses. Hence, this part of the data collection took longer than expected.
- Unable to find a suitable laboratory to process the samples
- Unable to confidently visualise the DJ flexure in older children
- 35% of patients have shown disease progression from initial assessment. Therefore a major amendment in the protocol allowing closer follow up of patients at 6 months on top of their 8 week and 1 year appointments has been implemented. This has also resulted in a retrospective analysis to help identify if there is evidence of disease progression and the effects on patient outcome. This raises the question to whether or not there are different levels of disease process in patients.
- A lot of work required to finalise trial protocol

➤ **Ethics approval**

- Re-working of licence constraints as required during the course of individual projects caused delay

- R&D approval from host institutions took longer than expected; delay in receiving ethics approval
- Process for having the study accepted onto the CLRN portfolio required additional approvals and paperwork
- Additional paperwork required to be completed for access to NHS datasets eg applications to relevant research committees
- In-vivo research is very difficult to organise in England
- Changes to Patient Information Sheet during the study which required amendments to the ethics approval

➤ **Changes in project team**

- Collaborator passed away suddenly so needed to recruit another clinician
- Principal Investigator (PI) moved location and ended up being a lot further away from the study site
- PI moved posts so the start of the project was delayed
- Main stakeholder was seconded away for 3 months which caused delay to progress of the study

➤ **Personal circumstances**

- Bereavement
- Physically demanding (e.g. no food/drinks allowed in imaging facility)
- Maternity leave
- Changed institutions retaining honorary contract at study site

➤ **Data analysis**

- Difficulty learning mathematical/computational aspects
- Support for data analysis required a lot of personal intervention as project was displaced by larger trials

➤ **Balancing clinical commitments and research**

- Challenging to spend sufficient time on the project within the limited time left in training
- Challenging to spend sufficient time on the project while preparing for and undertaking exams

➤ **Further funding was required**

- Delay in submitting for ethics review as all paperwork related to funding was required but took some time to obtain.