BAOMS

Research Update Report for Endowments sub-committee

Name: Mr Andrew Lyons

Title of project:
Can genomics predict dysphagia after head and neck radiotherapy?
A retrospective case controlled cohort study using Genome Wide Association (GWAS) to compare genomic differences between head and neck cancer patients who do and do not suffer from severe swallowing and mouth opening difficulties after radiotherapy or chemoradiotherapy.

Endowment meeting when grant was awarded: 26 March 2014

Date endowment grant was paid: £10,000 paid on 6 August 2015
£20,000 paid on 3 October 2016
£29,462 paid on 24 April 2018

The GRAD study is a pilot retrospective case controlled cohort study which aims to establish whether genetic markers can identify head and neck cancer patients who are at high risk of developing severe complications following radiotherapy or chemoradiotherapy. We hope to assess whether genome wide association studies (GWAS) can identify genetic variants, with the potential to stratify patients according to radiation hypersensitivity, and to assess whether saliva samples provide usable DNA for genetic studies on this group of patients.

The criteria are as follows:
Inclusion Criteria:
· Patients aged 18 years and over (no upper limit)
· Patients who have been treated for primary head and neck cancer with radiotherapy or radio-chemotherapy
· Patients who are between 1 and 6 years post-treatment

Exclusion Criteria:
· Those patients not deemed able to give informed consent
· Patients who have had thyroid cancer
· Patients who have had head and neck surgery

The study is ethically approved and was brought under HRA Approval in 2016. It has NIHR portfolio status, which means that NCRN research staff are assisting with the study in other research sites.

There are 13 research sites and 3 PIC (Participant Identification Centre) sites that are currently open and actively recruiting. The majority of these sites contacted the Trial Centre to join the study independently. These are: Barts, (PIC sites Guys, UCLH, and North Middlesex), Mount Vernon, Pennine, Portsmouth, Surrey, Walsall, Shrewsbury, Barking, Norfolk, Sheffield, East Kent, Nottingham and Cambridge.

In October 2017, a substantial amendment was submitted to change the protocol for Phase 2 of the study. The original Phase 2 consisted of 100 patients with severe swallowing complications and 100 patients with normal or mild to moderate swallowing complications being invited to research clinics where they would give blood and saliva samples, complete the MDADI questionnaire and complete a Repetitive Saliva Swallowing Test. The amended protocol includes the following:

- Invite all consented patients to attend a research clinic
- Patients who can swallow to complete the 100ml water swallow test
- Patients unable to easily produce a saliva sample will be given the option of providing a sample by gargling
- Patients will have their inter-incisal distance measured to assess limited mouth opening
- Patients will be graded as per the Fibrosis scale to grade the level of oedema/fibrosis after radiotherapy
- Patients will be asked to complete a repeat Sydney Swallowing Questionnaire
- Patients who are unable to attend will be asked to give a saliva sample that can be sent through the post

This amendment was approved by Ethics and the HRA. Currently, 11 sites have given R&D approval, 1 site (Norfolk) is unable to implement the amendment due to lack of capacity, and we are still waiting to hear back from 3 sites.

The 10 approved sites are:

Site name	**PI**	**Local contact**
Barts Health NHS Trust	Iain Hutchison	Sharon Cheung
UCLH	Dawn Carnell	Arti Kara
East and North Hertfordshire NHS Trust	Catherine Lemon	Lwazi Grinly
Portsmouth Hospitals NHS Trust	Debi Barnes	Debi Barnes
Royal Surrey County Hospital NHS Foundation Trust	Stephen Whitaker	Isobel Davies
Walsall Healthcare NHS Trust	Lynda Wagstaff	Susan Darby
Barking, Havering and Redbridge University Hospitals NHS Trust	Amy Ward	Morgan Brown
East Kent Hospitals University NHS Foundation Trust	Kannon Nathan	Katy Taylor
North Middlesex University Hospital NHS Trust	Anna Thompson	Chloe van Someren
The Shrewsbury and Telford Hospital NHS Trust	Laura Pettit	Emma Neeves
Cambridge University Hospitals NHS Foundation Trust	Richard Benson	Amy Bates

This amendment also requested to change Guys from a PIC site to a full research site. However, due to limited resources, it has been agreed with Guys R&D that research clinics will take place at Barts Health but some patients who are unable to attend will be seen by Andrew Lyons in his own time at Guys.

In July 2018 the study period was extended for a further year to August 2019 so that we could reach the target of 1,000 patients and have enough time to conduct Phase 2 of the study.

By the end of August 2018, 1,011 patients have consented to the GRAD study. Sites are still recruiting as some of these patients will unfortunately have passed away between consenting to the study and Phase 2 being conducted. In August 2018, Andrew Lyons (Guys) produced a list of new patients and these patients were screened to see which of these are eligible to be invited to join the study. Invitations will be sent out in September 2018.

We have started to organise the research clinics to be held at Barts. Suitable locations are being investigated, and one at The Royal London has been identified. We no longer need to identify the “poor” and “good” swallowers as all eligible patients will be invited to the research clinic, and our Trial Co-ordinator has started to telephone patients to find out when they are available. We will conduct the GWAS on batches of 40 blood and saliva samples at the Barts Genome Centre as patients are called in and seen.

We will hold a pilot research clinic at Barts so that written instructions can be given to the sites that have approved the substantial amendment before they commence holding research clinics. Staff required for the clinic include one clinician, one phlebotomist and one clinical researcher.

Costs for the location at The Royal London are £80 per day for the clinic rooms, and £12 per blood sample collected by the phlebotomist.

In February 2018, a minor amendment was submitted to add 2 new research sites. One of these, Cambridge, is fully set up and running and have recruited patients. The other, Maidstone, has had R&D approval but is still waiting for site initiation dates from the PI.

The data collected so far is fascinating for the proportion of patients who appear to have died following radiotherapy or chemoradiotherapy. This information has the potential to lead to future developed and approved studies on this cohort of patients.

Money spent to date (include separate receipts and brief details on how the money has been spent):

The grant awarded from BAOMS is meant solely for the GWAS analysis, which will take place later this year. Saving Faces has funded staff time, purchase of study materials and postage costs. We have also been responsible for collecting and entering data for the PIC sites, and telephoning patients.

Anticipated date of when paper will be submitted to BJOMS for possible publication:

We should be able to publish details of the patients treated with primary Radiotherapy (plus or minus chemotherapy) and their outcomes at all sites and the GWAS study in a separate paper in early 2019. As well as publication in BJOMS we would aim to publish in parallel in a high impact journal. These

articles would cross-reference each other probably drawing in more readers and citations to the BJOMS article.