

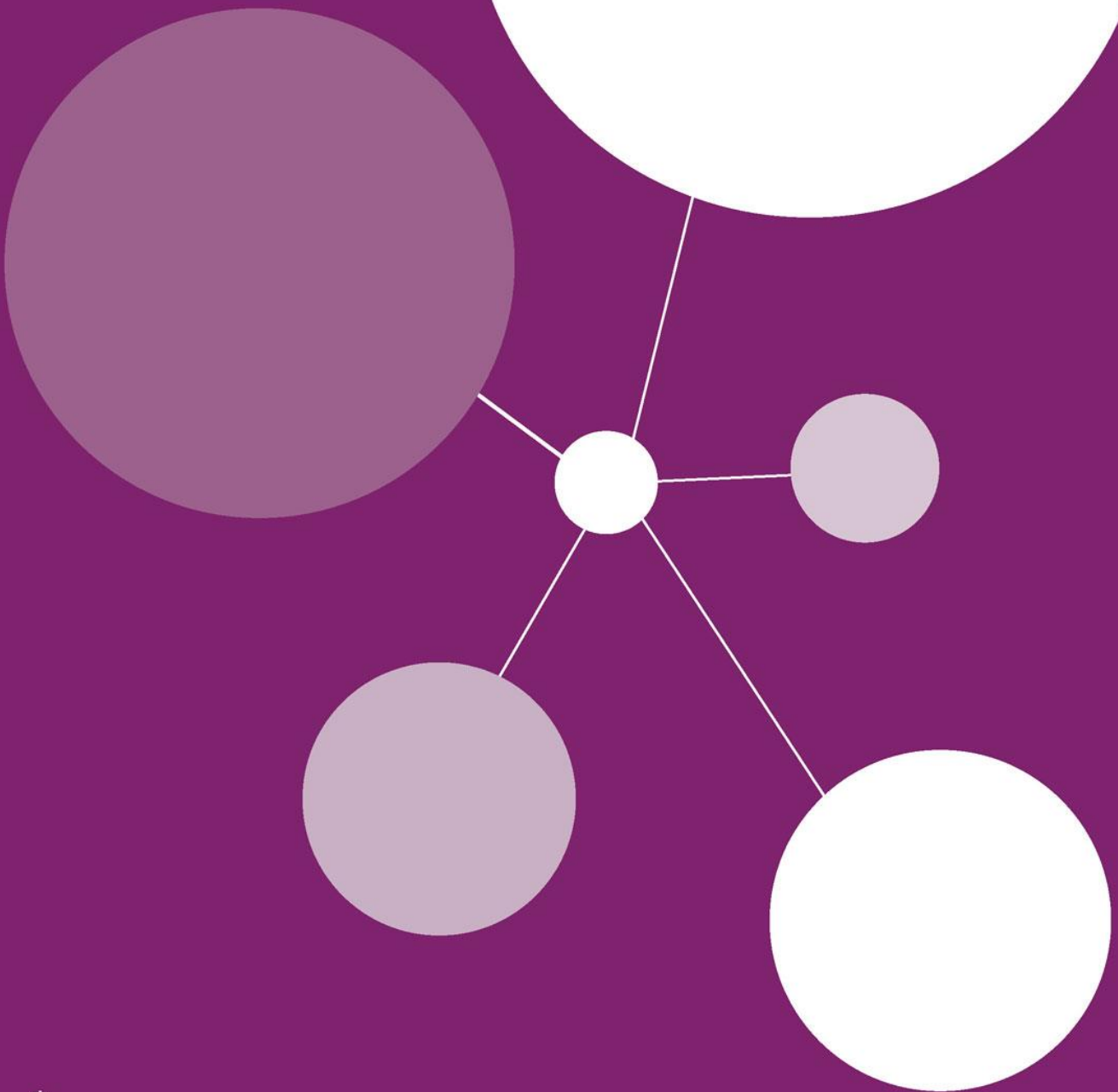


**NCRI**

National  
Cancer  
Research  
Institute

# **NCRI Prostate Group**

**Annual Report 2019-20**



Partners in cancer research

**The NCRI Group Annual Reports 2019/2020** span the time period April 2019 – March 2020. The reports were submitted during a challenging time for all in the healthcare sector due to the COVID-19 pandemic. This has had an unprecedented impact on the activity of both the Research Group itself and wider research activities, ranging from the time available for research work versus clinical commitments to the funding of new trials and the recruitment of existing trials. Due to this the NCRI significantly extended the deadline for submission of annual reports and allowed the Groups to submit reduced reports, if time permitted, with the following sections at a minimum:

- Achievements (section 1 of the report)
- Funding Submissions over the last 12 months (section 5)
- Priorities and Challenges (section 7)

In addition to this, Consumer representatives of each Group were asked to only complete their sections if they feel able to. Most of our Consumers have submitted reports, however where reports have *not* been submitted this was due to extended periods of ill health, or additional work/home life constraints, as a result of COVID-19.





## NCRI Prostate Cancer Group Annual Report 2019-20

### 1. Top 3 achievements in the reporting year

#### **Achievement 1**

RADICALS-RT (CI: Chris Parker) reported its 5 years outcomes at ESMO in September 2019. It showed no difference between cancer recurrence in men given early radiotherapy (adjuvant) versus those given salvage radiotherapy. The results of the RADICALS-RT trial were confirmed by the ARTISTIC meta-analysis which included the RADICALS-RT data in a 3 trial collaboration.

#### **Achievement 2**

The IP1-PROSTAGRAM study showed that a community-based screening MRI in the community might detect more significant cancers without increasing the biopsy rate. Alongside the pilot BARCODE-1 study also presented at ASCO, these results indicate the role for new smarter screening studies for future full evaluation.

#### **Achievement 3**

A balanced portfolio between the two subgroups, with ongoing cross-fertilisation between NCRI groups, with success in three applications to CRUK Clinical Research Committee for potential practice-changing studies and a further 3 shortlisted studies to other funders.

### 2. Structure of the Group

#### Prostate Cancer Group & Subgroup Strategies

##### Prostate Cancer Group

**Minimise the harms from the investigation and treatment of localised prostate cancer**

**Maximise the quality of life and overall survival of patients with advanced prostate cancer**

**Promote a clinical research culture within urology which encourages young urologists to develop an interest in clinical trials**

**Promote international collaborations on prostate cancer trials**

**Foster links with the British Uro-oncology Group (BUG) and the British Association of Urological Surgeons (BAUS) Section of Oncology**

**Work with the Bladder & Renal and TYA & GCT (the Testis CSG has merged with the TYA CSG) CSGs to encourage clinical research in the uro-oncology community**

**Foster a harmonised approach to tissue biomarker collection for future translational studies accompanying clinical trials**

**Strengthen links with Prostate Cancer UK**

### **Advanced Prostate Cancer Subgroup (Chair, Gert Attard)**

**Build on the success of STAMPEDE, introducing new treatment comparisons into the trial**

**Identify intermediate endpoints to hasten clinical development of new agents**

**Collaborate with the Supportive and Palliative Care CSG**

**Focus on translational science with an overarching focus to progress the theme of personalized medicine in advanced prostate cancer**

**Engage with the Experimental Cancer Medicine Centres (ECMC) network**

### **Localised Prostate Cancer Subgroup (Chair, Rakesh Heer)**

**Evaluate strategies to reduce the over-diagnosis and over treatment burden in localised prostate cancer**

**Evaluate strategies to improve current treatment**

**Encouraging trials with value added secondary themes of biobanking and health service research**

**To encourage, nurture and enable young/new investigators to the field**

### **3. Task groups/Working parties**

The Prostate Cancer Group had no task groups or working parties during the reporting year.

#### 4. Funding applications in last year

**Table 2 Funding submissions in the reporting year**

Study	Committee & application type	CI	Outcome	Level of Group input	Funding amount
<b>Cancer Research UK</b>					
<b>May 2019</b>					
Local therapy with or without metastasis-directed therapy in oligometastatic prostate cancer-- an additional comparison within the STAMPEDE trial	Amendment	Professor Nicholas James	Conditionally supported	Full input at advanced subgroup (Chair: Jones) and then 1-2 hour discussion at main group meeting. Full minutes of meeting shared with CRUK CRC committee.	
<b>November 2019</b>					
RADICALS: Radiotherapy and Androgen Deprivation In Combination After Local Surgery	Clinical Trial Award - Amendment	Dr Chris Parker	Supported	Reviewed and supported by Localised Subgroup and main group prior to and after submission of application. Interim results shared confidentially with Chairs (Ahmed, Heer)	
PEARLS: A phase II/II trial of Primary radiothErapy for Androgen sensitive pRostate cancer patients with Lymph nodeS	Clinical Trial Award	Dr Julia Murray	Supported	Fully discussed and supported by Advanced Subgroup (Chair: Attard).	

Aggressive prostate cancer: understanding the aetiology through worldwide epidemiological and interdisciplinary collaborations	Programme Award	Professor Timothy Key	Not submitting		Year 1 commitment: £1,032,365 (£2,817,576 full)
<b>Other committees</b>					
Evaluating the role of fast MRI and image-fusion for detection of prostate cancer	Cancer Research UK – Population Research Committee	Professor Hashim Ahmed/Professor Rhian Gabe (NCRI Primary Care Research Group)	At full application stage; full review suspended until Autumn 2020 due to Covid19 pandemic	Fully developed by NCRI Prostate and Primary Care group members. Multiple levels of input by Localised Subgroup with feedback prior to funding submissions. Heer is co-applicant. Derek Price is one of two PPI co-applicants.	
<b>Study</b>	<b>Committee &amp; application type</b>	<b>CI</b>	<b>Outcome</b>	<b>Level of Group input</b>	<b>Funding amount</b>
A randomised controlled trial of TRANSrectal biopsy versus Local Anaesthetic Transperineal biopsy Evaluation (TRANSLATE) of potential clinically significant prostate cancer.	NIHR HTA Randomised controlled trial	Mr Richard Bryant, Oxford	Shortlisted (final outcome awaited)	Review by Localised Subgroup and main group with full presentation and feedback by trials team. Input into design and areas of contention by Chair (Ahmed) directly via email and verbally to Oxford team. Lead	£1-2M (outcome awaited for end July 2020)



				applicant Bryant is a new member of the NCRI Prostate Research Group.	
The clinical and cost-effectiveness of biparametric MRI compared to multi-parametric MRI in detecting clinically significant prostate cancer	NIHR HTA Randomised controlled trial	Professor Hashim Ahmed/Professor Rhian Gabe (NCRI Primary Care Research Group)	Shortlisted (final outcome awaited)	Fully developed by NCRI Prostate and Primary Care group members. Multiple levels of input by Localised Subgroup with feedback prior to funding submissions. Heer is co-applicant. Derek Price is one of two PPI co-applicants.	£1.7M (outcome awaited for end July 2020)
A study to assess the clinical and cost-effectiveness of the Ibox Artificial Intelligence Histology system in diagnosing clinically important prostate cancer on prostate biopsy tissue	NIHR AI awards Prospective paired cohort validation study	Professor Hashim Ahmed/Dr Adam Brentnall (QMUL)	Shortlisted (final outcome awaited)	Academic-commercial collaborative project. Developed with input from NCRI Prostate Localised Subgroup and NCRI CM-Path group.	£600,000 (outcome awaited for end July 2020)
The Neurosafe Randomised Controlled Trial	JP Moulton Foundation. Full study award	Mr Greg Shaw, UCL/QMUL	Awarded	Reviewed and feedback provided by NCRI group and Chair during pilot set-up and when pilot succeeded in obtaining NIHR-RfPB funding (~£250K)	£600,000

CHOICE: Understanding decision making for active surveillance	The Urology Foundation	Athene Lane, Caroline Wilson, Prasanna Sooriakumaran, Jon Aning	Not awarded	Reviewed and feedback provided by NCRI Localised Subgroup	£85K
Putting men's preferences at the center of the doctor-patient relationship: The Prostate cAnceR TreatmeNt prEfeRences (PARTNER) Test	The Urology Foundation	Verity Watson	Awarded	Reviewed by NCRI Chair and co-applicant on grant	£35K

## 5. Consumer involvement

Ms Sue Duncombe and Mr Derek Price have been members of the NCRI Prostate Research Group since summer 2016 and are both in their 2<sup>nd</sup> term as consumers on the group. Sue joined the Advanced Disease Subgroup 18 months later and Derek joined the Localised Disease Subgroup at the same time. They have made active contributions particularly to sub-group meetings, where more practical issues of studies are discussed.

Derek and Sue communicate regularly to exchange information, ideas and opinions about current research and issues in prostate cancer and feedback from meetings. When providing feedback on studies by email to investigators or Prostate Group Leads they collaborate to provide one set of consumer feedback.

The trials which they have provided most significant feedback on this year have not yet received funding approval so they are not referred to here by name. Giving a couple of examples – one was looking at identifying modifiable risk factors in aggressive prostate cancer and another looking at M0/M1 patients with updated SOC for prostate cancer. Both investigators recognized the value of the consumer input and included it without change in their submission. In addition, one of the mentors commented that it was ‘a very thorough review’.

At a Dragon's Den concerned with improving radiotherapy for a number of different cancers, they were able to contribute by commenting on the potential value of the study for prostate patients. By the end of the meeting the researcher recognized that they would not need to provide technical details of tests to patients, just the implications of the test results for treatment.

Their involvement with Cancer Research UK (CRUK) (Sue) and Prostate Cancer UK (PCUK)(Derek) enables them to bring a wider perspective and knowledge to the Prostate Group which also benefits their activities with the charities.

### Derek Price

Derek Price has, as a result of a medical condition, been restricted in his involvement in activities for a significant part of the year. He was also unable to attend a number of NCRI meetings or be involved in PCUK awareness-raising or hub group activities.

He continues to be a member of the PCUK Public and Patient Involvement (PPI) group which comments on research applications and their implications for patients and is then presented to the Research Advisory Committee.

As a member of CORE, ATLANTA, and PROSTAGRAM TMGs he has had input into meetings and has provided feedback on various materials. He has recently been appointed to two additional TMGs (one being the PACE trial). Derek is particularly interested in research involving early diagnosis of prostate cancer and the treatment of advanced disease, and these trials all allow him to input into these areas.

He is a member of the National Prostate Cancer Audit PPI Forum and has been involved with reviewing materials to make them more accessible and relevant to patients.

He keeps members of his local support group aware of current research issues and e.g. encourages them to participate in research surveys when relevant.

### **Sue Duncombe**

Sue has attended all meetings (F2F and Zoom) of the main group and advanced disease Subgroup, in addition to the NCRI conference She was scheduled to attend the Urological trial day, but this was cancelled.

At the advanced disease Subgroup meeting there was discussion about developing guidelines for restarting clinical trials following the COVID-19 pandemic. Her input on the benefit for patients of having such guidelines communicated were described as very useful by the sub-group chair and shared with the Prostate Group lead.

Mr Rakesh Heer is Sue's mentor. Whilst there is not very frequent contact, Mr Heer is always available when required and responds promptly to any queries.

Whilst some of Sue's activities outside of the NCRI Prostate Group support more general areas of oncology, this work can ensure the environment for research is positive and also improves the chances that the Group's work can be implemented in the NHS. She has campaigned on behalf of CRUK by meeting her MP and by communicating with Ministers to ensure cancer was a priority in the general election, that research is a priority in Brexit negotiations and for the government to address issues in the diagnostics' workforce.

She is a member of a the National Institute of Health Research (NIHR) Study Dissemination Information working group to develop guidelines for sharing study results with patients, or in event of their death, their next of kin, an area she feels passionate about.

## 6. Priorities and challenges for the forthcoming year

<b><u>Priority 1</u></b> To develop a strategy through a pan-NCRI Prostate and Primary Care alongside major funders approach to develop and obtain funding for the next generation screening trial.
<b><u>Priority 2</u></b> To structure and commence activities of a working group that will enable the use of national data within longitudinal trial outcomes.
<b><u>Priority 3</u></b> To develop, fund and deliver novel arms within STAMPEDE, particularly focused on stratified approaches.
<b><u>Challenge 1</u></b> Restarting and recruiting to viable clinical trials nationally within the challenges brought by COVID-19 (CRN support, prioritisation and recovery plans locally differ in each Trust, decreased GP referrals of suspected cancer will lead to significant decreases in pool of eligible patients).
<b><u>Challenge 2</u></b> Significant decreases in charitable donations during COVID-19 have already led to prioritisation of existing studies that are viable rather than considering new studies.
<b><u>Challenge 3</u></b> Clinical demands on all clinical group members as recovery plans for dealing with clinic and treatment waiting lists.

## 7. Collaborative partnership studies with industry

The STAMPEDE group (CI: Professor Nick James) continue to work with commercial pharmaceutical companies to identify and support new drugs for evaluation.

The reIMAGINE study (CI: Emberton; co-PIs: Professor Hash Ahmed/Professor Gerhardt Attard/Professor Caroline Moore/Dr Mieke van Hemelrijk) (funder: MRC/CRUK) now has over 20 commercial collaborators and approximately 1-2 new partners apply to join every quarter.

A recent collaboration between Ibx Medical who have developed an Artificial Intelligence (AI) tool to evaluate histology automatically is currently undergoing review by the NIHR AI stream of funding. This pan-NCRI group (Prostate and CM-Path) evaluated proposal is hoped to be the first of many in this emerging area.

## **8. Appendices**

Appendix 1 – Prostate Cancer Group strategies

A – Advanced Prostate Cancer Subgroup Strategy

B - Localised Prostate Cancer Subgroup Strategy

Appendix 2 – Top 5 publications in reporting year & Group involvement with NICE appraisals

**Professor Hashim Ahmed (Prostate Cancer Group Chair)**

## Appendix 1

### Prostate Cancer Group strategies

#### A – Prostate Group Strategy

##### Overall goals

1. To minimise the harms from the investigation and treatment of localised prostate cancer.
2. To maximise the quality of life and overall survival of patients with advanced prostate cancer.

##### Aims

- To promote a clinical research culture within urology which encourages young urologists to develop an interest in clinical trials.
- To promote international collaborations on prostate cancer trials.
- To foster links with the British Uro-oncology Group (BUG) and the British Association of Urological Surgeons (BAUS) Section of Oncology.
- To work with the Bladder & Renal and TYA & GCT (the Testis CSG has merged with the TYA CSG) CSGs to encourage clinical research in the uro-oncology community.
- To foster a harmonised approach to tissue biomarker collection for future translational studies accompanying clinical trials.
- To support consumer involvement in clinical research and establishing links with the Prostate Cancer Support Federation.
- To strengthen links with Prostate Cancer UK.

## **B – Advanced Disease Subgroup Strategy**

### **Aims**

- To focus on translational science with an overarching focus to progress the theme of personalised medicine in advanced prostate cancer.
- To engage with the ECMC network.
- To build on the success of STAMPEDE, introducing new treatment comparisons into the trial.
- To identify intermediate endpoints to hasten clinical development of new agents.
- To collaborate with the Supportive and Palliative Care CSG.
- To identify and address knowledge gaps where the UK has a unique opportunity to bring change.



## **C – Localised Disease Subgroup Strategy**

### **1. Evaluate strategies to reduce the over-diagnosis and over treatment burden in localised prostate cancer**

#### *Project 1: Screening MRI in the community*

The Subgroup discussed, developed and worked up (with the Chair as CI) to successfully gain funding from the Wellcome Trust (£2.1M; 2017-22) to develop and deliver a screening study using multi-parametric MRI (T2W and diffusion only) in the community with a primary focus on high risk men, e.g. African and African-Caribbean men, family history. The study will start in Q4 2017 and aims to recruit between 1,000-2,000 men.

#### *Project 2: Validation of Stockholm-3 panel*

The Subgroup has worked with the SPED Advisory Group and Primary Care CSG to develop a protocol and application for funding to conduct a validation study in the UK of the Stockholm-3 biomarker panel. The Chair, Rhian Gabe (York) and Fiona Walters (Cambridge) (both from NCRI Primary CSG, Walters and Ahmed from the NCRI SPED) will be co-leads of this project. At the time of writing, Prostate Cancer UK have shortlisted and interviewed our team as the preferred bidder and we are in further discussions about the next stages of changes prior to a final decision on funding. We expect this study to recruit 20,000 men in the community.

#### *Project 3: re-IMAGINE proposal*

We have worked with Professor Mark Emberton (UCL) to help the consortium he successfully led for an MRC Stratified Medicine bid. It aims to recalibrate the current risk tools we have in localised prostate cancer which are based on Transrectal biopsy to one that is based on upfront multi-parametric MRI and targeted biopsies.

### **2. Evaluate strategies to improve current treatments**

#### *Project 1: Neurosafe technique to reduce surgical margins*

We are working with a new PI, Greg Shaw (UCL), to develop a protocol to comparatively evaluate a new surgical technique which might improve nerve-sparing surgery during radical prostatectomy called Neurosafe. This is being worked up for a feasibility/pilot study.

#### *Project 2: Strategies to minimize cardiovascular toxicity of hormones during radiotherapy*

We are working with Ann Henry (Leeds) who is also working on funding for a comparative randomized study to evaluate strategies to minimized cardiovascular toxicity of hormones during radiotherapy.

#### *Project 3: Using mpMRI after radiotherapy to predict long term failure*

We are working with Anita Mitra (UCL) who has now obtained pilot funding to determine whether immediate post-radiotherapy mpMRI might predict long term outcomes.

*Project 4: CHRONOS - Focal therapy Multi-arm Multi-Stage RCT*

The role of ablative therapies is increasing and might be a strategy to reduce the harms of therapy in a select group of men who require treatment and would normally have surgery or radiotherapy. The Chair, Melissa Williams and Matt Sydes (MRC CTU), alongside the EORTC-GU group and one of the CSG trainee representatives (Taimur Shah), worked on an MAMS RCT design to evaluate neoadjuvant and adjuvant strategies with focal ablative therapy. This has been combined with a PACE style preference based RCT design with a direct comparison of radical therapy with focal therapy as well as the focal MAMS RCT. This has been funded in pilot by Prostate Cancer UK.

*Project 5: PART study*

An RCT of partial ablation looking at using VTP versus radical treatments for unilateral intermediate risk prostate cancer. The full application is going through its second iteration with the NIHR HTA panel now (Freddie Hamdy, Oxford).

*Project 6: The 5-3-1 study*

Innovative MR-guided adaptive radiotherapy regimes will be studied, including the potential for a one off treatment (Alison Tree (ICR) and Choudhury Ananya (NHS Christie))

**3. To evaluate methodological strategies to improve accrual and success of comparative surgical research.**

This aim primarily concerns surgical research. We have seen countless RCTs of surgery in prostate cancer, but also in bladder and renal cancer, where RCTs evaluating strategies compared to surgery were proposed as the intervention arm. Novel trial designs and methods are needed. The Chair is working with members of the CSG such as Matt Sydes to evaluate novel trial designs such as the MAMS design (see above), as well as other designs such as the cohort-multiple RCT described by Jon Nicholls and Clare Relton from Sheffield.

**4. Encouraging trials with value added secondary themes of biobanking and health service research**

*Project 1: PREVENT trial*

Stockholm3 index validation study full submission to second round PCUK review – will include biobanking for biomarker studies (supporting potential follow on funding).

*Project 2: PROVENT*

A randomised, double blind, placebo-controlled feasibility study to examine the clinical effectiveness of aspirin and/or Vitamin D3 to prevent disease progression in men on Active Surveillance for prostate cancer (Greg Shaw and Jack Cuzick (UCL)).

*Project 3: CTC study*

The exploration of novel non-invasive liquid biopsy approaches for prostate cancer diagnosis - aims to develop an efficient circulating biomarker model for non-invasive triage/diagnosis of clinically significant PCa. We will combine the CTC and CtRNA analyses in a same cohort of pre-biopsy patients with mpMRI data to improve the accuracy of non-invasive triage for biopsy. CtDNA (methylation) and CTC RNA expression will also be explored in the same samples for their triage/diagnostic value (Lu Yong-Jie and Hayley Whitaker, Queen Mary and UCL).

**5. To encourage, nurture and enable young/new investigators to the field.**

We have started to help and encourage a number of new PIs in the field including Rhian Gabe, Anita Mitra, Ann Henry, Greg Shaw, Taimur Shah, Paul Cathcart and Declan Cahill in a robust but supportive manner. We hope those not part of the CSG will apply to become Localised Disease Subgroup members and, in time, some of the Subgroup members will apply to become main CSG members. This will be in tandem with working up their own ideas, protocols and grant submissions.