# Evidence Brief

## FASTMAN I & II - Manchester/Belfast Movember Centre of Excellence

### Why did we start? (The need for the research and/or Why the work was commissioned)

The FASTMAN Centre of Excellence has been transformative for prostate cancer research in Belfast and Manchester. It has enabled the development of a large multidisciplinary team of research experts (clinical, molecular biology, radiobiology, bioinformatics, genomics, pathology, physics), many of whom were new to prostate cancer research, to focus on a central hypothesis addressed through a number of linked work packages. New talent has been recruited with the result that prostate cancer and radiation research have become a major focus of both institutions.

### What did we do? (Methods)

In the first five years FASTMAN (2015-2019) concentrated on "Discovery Science" to understand the context of locally-advanced prostate cancer, the activation/modulation of genetic/biological pathways in response to stress induced by radiation exposure and how they contribute to the differential sensitivity of therapeutic response. In FASTMAN 2 the focus was on "delivering this impact to men" by focusing on the application of previous discovery to patients. (The covid-19 pandemic led to some very challenging delays in the FASTMAN programme.)

### What answer did we get? (Findings)

The team continue to make discoveries in key areas of prostate cancer by focusing on research into the most serious form of the disease and by working with researchers from multiple disciplines including oncology, urology, physics, biology, genomics and big data.

**ADRRAD**

- A new way to measure disease response in bone metastases using MRI
- A link between the amount of DNA damage in the white blood cells and the patient benefit from Radium treatment
- Changes in the chromosomes of patients treated with Radium

**SPORT**

- First randomised clinical trial comparing prostate SBRT to prostate and nodal SBRT
- Preliminary data for the Phase III PACE NODES trial
- Two biomarkers appear to predict for patients likely to develop toxicity – yH2AX and citrulline
- Use of a peri-rectal spacer in patients treated with SBRT. This informed a global trial exploring a novel contrast-enhanced spacer in patients treated with prostate SBRT.

**HYPROGEN**

- Recruited 4 patients to ARM A (M1 patients) with paired primary and bone metastases and ctDNA and CTC samples.
- Success with Visium10X spatial transcriptomics for both types of samples and pairing this with PIMO and GLUT-1 IHC to describe transcriptomes in oxic and hypoxic areas.
- Ethics and contracts approved for Arm B of the Hyprogen trial (radical prostatectomies in high risk patients) to open imminently.
- Success in growing primary prostate epithelium with hTERT-immortalisation to drive new models from aggressive high-risk patients with hypoxia.
- Progress in the STAMPEDE imaging sub-study. Images retrieved and analysed for Arms A,C,E, G & J. The study has been expanded to retrieve and analyse patient data from comparisons A/K and A/L.

**PRC**

- Established a novel patient sample platform (PRC) enabling us to understand how treatment impact evolution of prostate cancer and recurrence and will allow us to identify novel treatments to improve efficacy of standard of care radiotherapy based treatments.

### What should be done now? (Practice/Policy Implications and/or Recommendations)

The outputs from this research has been presented at international meetings and will be published in the open scientific literature so that scientists and clinicians can access this. Further funding is being sought from Prostate Cancer UK to build on our highly successful FASTMAN programme (2015-present) and to build on the well-established collaboration between Queen's University Belfast and the University of Manchester. Our team of internationally recognised prostate cancer researchers are very well placed to advance the field of imaging and circulating biomarkers for escalated bio-adapted radiotherapy in prostate cancer.