Centre for the Clinical Application of Particles

Management Board Meeting #1

Room 532, Level 5, The Blackett Laboratory, Imperial College London
Tuesday, 06Jun17, 16:00 – 18:00

Present:

Matt Williams (phone), Eric Aboagye, Ken Long, Mark Hill, Boris Vojnovic, Jürgen Pozimski, Dan Elson, Andrei Seryi, John Yarnold, David Colling, Jaroslaw Pasternak, Zulfikar Najmudin, Dorothy Gujral (phone), Piero Posocco, Jennifer Podesta (phone), Victoria Blackmore

Apologies:

Danielle Power, Charles Coombes, Uwe Oelfke

Notes:

1. **Welcome, introductions and goals for the meeting**

KL thanked everyone for agreeing to serve on the Management Board (MB) and for attending this first meeting. KL also thanked everyone for the contributions to the proposal to establish the CCAP that had recently been submitted and for the contributions to the two proposals (PhD student and £30k CRCE pump-priming funds). Each member of the MB present or on the phone introduced themselves; KL added some words of introduction for the few MB members unable to attend.

The goals for this, the first, meeting of the MB would be to discuss the ambitions that have been defined for the CCAP and to identify a small number of topics aligned with our ambitions that we can develop in the short term.

2. **CCAP: status of application, aims and objectives, discussion**

The formal proposal for the establishment of the CCAP at Imperial had been submitted. The result was expected to be announced by the end of June 2017.

EA commented that this was a unique programme internationally. BV and MH agreed that there are very few groups internationally that are working in this area. The study of the biological impact and relevance of particle beams was felt to be of value, though the equipment that would be required was felt to be expensive.

The meeting's attention was drawn to the organigram. The roles and composition of the various bodies described in the proposal was discussed and the membership of the MB was noted. It was noted that the Imperial rules require a truly independent External Advisory Board (EAB). While the CCAP is in its formative phase, it was proposed to use the Advisory Board of the CRCE to fulfil the EAB role. The Governing Board (GB) had been conceived as the "stakeholder body" composed of the heads of the various institutes and departments that make up the CCAP. Since the bulk of the GB is ex-officio, it is proposed that the GB be established if and when the CCAP is approved and the Centre has begun to work. The MB had been assembled and includes two persons per institute, department or group.

3. Summary of initial discussions with MB members

In preparation for the meeting, KL and VB had discussed possible initial directions for the CCAP programme with MB members. A short summary of these discussions had been circulated to the MB ahead of the meeting.

The summary document was discussed. The following suggestions for modifications and corrections were made:

- Greater clarity may be achieved by grouping possible research topics into themes: cell-based, animal-based, and potential clinical developments;
- The Faculty of Medicine (EA) has an existing collaboration with the Institute of Data Science rather than the Department of Mathematics. The reference to "internal beam (beta source)" should be changed to "radionuclides", the markers are fluorescent rather than phosphorescent and the programme described seeks to quantify cell response to dose deposition (rather than dose rate);
- The CRUK Centre has a budget for cancer-related activities at Imperial. It is able to facilitate funding applications and access to data. The Centre has a registry of people working on Cancer at Imperial. MH asked whether data on the ablation products of the iKnife might be made available; DE said that this was probably possible;
- MW noted that 4—5 treatment-planning packages are in use clinically across the country. There is a need for "configurable" planning s/w. In this context, the Monte Carlo simulation of particle/tissue interactions was discussed. BV commented that the Geant4-based "GATE" package should be investigated and that there may be open-source s/w tools, one originating in Heidelberg. **BV** will forward a list of such packages to the MB. In addition, FLUKA and MCNP are used. The application of such packages to continuously-variable energy (photon) IMRT and VHEE was of interest (MW). Packages such as "OpenRad" are in use at ICR. **JY** will ask UO about the software that is presently available at the ICR;
- MH and BV pointed out the importance of "end-point" studies to localise the position of the Bragg peak. A good simulation would be important in this context;
- OIRO research is primarily on drugs that modify the radiation response of a cell. The OIRO also has some practical tools for micro-dosimetry of cells (at the level of nm dose-deposition); and
- We agreed to survey the available treatment-planning software (**VB**).

The value of updating the summary document and then circulating it for further correction and refinement was discussed and agreed (action **VB**).

4. Discussion of initial foci for development of research programme

The excellent discussion was wide-ranging; the principal topics may be reported in three classes:

- *Systematic study of the radiobiological impact of particle beams:*

  Some of the points made during the discussion are noted below.
  - JY noted that we must distinguish our activity from other UK and non-UK collaborations active in this area.
  - RBE at the back of the treatment volume is one of the big questions in proton therapy;
  - MH noted that there is already a lot of work in progress using PET/SPECT with protons and it may be hard to compete in this area;

- JPa noted that our ultimate goal must be to have a unique, compact source of multiple particle species;
- ZN noted that there are several sources across the country that could be exploited if travel is an option;
- It was noted that access time at existing facilities may be an issue since biological experiments often require to be repeated and so exceed the time allocated for a particular exposure; and
- It was ***agreed*** that multi-species radiotherapy is an interesting area to develop as is LET-painting, using different particles.

It became clear during the discussion that there is a requirement to define the 5-year timetable for measurements and the likely timetable on which various beams can be delivered (requested by EA).

ZN summarised the possible evolution of laser-driven beams. At RAL, it is possible to gain access to 1 GeV electrons at low repetition rate, or 150 MeV electrons at 5 Hz. At RAL, protons can be delivered with a broad energy spectrum up to 40 MeV with a rep rate of 1 shot every 20 s at present. In the basement of the Blackett Laboratory, protons of energy up to 5 MeV should be available by the end of the summer. Once the delivery of protons has been proven, it should be possible to move on to heavier ion species. The energies and rep-rates were felt to be useful for cell work.

- *Imaging and diagnostics:*
  - The importance of determining the position of the Bragg peak, ideally during irradiation, was identified. In particular, one of the advantages of proton therapy is its use in the vicinity of sensitive organs, so it is critical to control the position of the Bragg peak. DC has simulated (using Geant) the photons that are emitted in the nuclear processes that occur just before the Bragg peak. It may be possible to identify the photons and "point back" to the position at which they were produced. Dose-deposition measurements are also of value and would require a wide variety of expertise to deliver a decisive programme;
  - EA is studying novel PET tracers to look at cardiovascular damage from radiotherapy. DG is researching the use of ultrasound to look for early biomarkers for radiotherapy damage; and
  - BV noted that there is a lot of clinical data available that should be compared with simulation. The "what if" questions, for example, mitigations for patient movement, can also be addressed by simulation. This topic is also believed to be of interest to UO.
- *Development of compact, laser-driven, novel-post-accelerator facility:*
  - AS argued that a specification of the requirements on the beam for a useful/definitive measurement programme is required. The discussion proposed the following indicative specification:
    - Beam energy in the range 30—50 MeV;
    - Capability to deliver 1 Gy/minute, and
    - Support for measurements of normal-tissue response.
  - The availability of laser-driven beams outlined by ZN is noted above. This partially fulfils EA's request for a timeline for the availability of beams. MH and BV noted that the ability to irradiate mice must form part of the

specification since facilities in which in-vivo studies can be performed are uncommon.

The discussion condensed the three classes of research outlined above to two themes:

- Radiobiology; staged, incremental programme of measurement supported by simulation; and
- Development of laser-source with novel post-acceleration system for radiobiology.

We ***agreed*** that two dedicated meetings in the style of IOP half-day meetings would be organised to work-up and agree a specification for the themes. It was ***agreed*** that in preparation for these meetings short discussion documents would be prepared to catalyse discussion and to be refined and developed as a specification of our programme (action **KL**). **KL/VB** would organise these meetings and bring together between 2 and 4 MB members to take the lead in drafting the discussion documents.

5. Future meetings

We ***agreed*** to organise the following meetings:

- *CCAP "plenary meeting":* this would be organised by Doodle and, ideally, would take place before the start of the next academic year in September 2017 (action **VB**);
- *Peripatetic Seminar series:* we ***agreed*** to initiate a regular series of seminars that rotates among the institutes that form the CCAP (action **KL/VB**). The seminars would be widely advertised in the institutes. **MH** also proposed to invite CCAP members to take part in the MSc course he runs at OIRO; and
- *Clinician-led meeting*: the goal of the meeting, proposed by CC, is to allow clinicians to bring forward and discuss issues arising from the clinical use of particles. The scope would include radiotherapy, treatment planning, imaging, image processing etc. **MW** and **DG** volunteered to organise the meeting.

In addition, a dedicated discussion of simulation codes and their development would be valuable.

6. Opportunities for development of links with appropriate industry

Contact had been made with R. Wilson, Head of Corporate Partnerships, Faculty of Natural Sciences. She had made a summary of industrial connections that may be valuable. This information would be circulated (action **VB**).

7. Outcome and feedback from two proposals made to date

Principal issue with both the proposal for a PhD student and CRCE pump-priming resources was the fact that detailed deliverables in the context of a broader programme were not specified. It is now important to articulate our programme such that elements of it can be abstracted to form the basis of proposals. In addition, we need to target appropriate programme grants against calls, for example, from EPSRC. This will be a focus going forward.

8. Date of next meeting

The date of the next meeting will be organised through a Doodle polls (action **VB**).

9. Summary of actions

The principal actions from the meeting were summarised. The full action list is appended to the notes of the meeting.

10. Any other business

- MW summarised the outline for a paper that he had circulated before the meeting. The idea was to summarise the benefits that would accrue from changes in performance of particle-based equipment. All ***agreed*** to review the content of the proposed paper and **MW** agreed to push the idea forward.

Summary of actions

- **BV:** Circulate list of s/w packages that simulate the passage of particle beams through tissue;
- **JY:** Circulate list of simulation packages presently in use within the ICR to simulate particle interactions with tissue;
- **VB:** survey the available treatment-planning software;
- **VB:** Incorporate comments in the summary document tabled at the meeting and circulate for further amendment;
- **KL:** Seek volunteers to draft discussion documents outlining the programme to be carried out in each of the two themes outlined above;
- **VB:** Organise "CCAP plenary meeting" in September 2017;
- **KL/VB:** Organise a "half-day" meeting to discuss the two themes outlined above;
- **KL/VB:** Initiate organisation of peripatetic CCAP seminar series;
- **MH:** Invite CCAP members to take part in the MSc course on radiobiology that he runs at OIRO;
- **MW/DG:** Organise "clinician-led" CCAP programme-development meeting;
- **VB:** Circulate summary of industrial connections from R. Wilson
- **VB:** Identify date and time of the next MB meeting by Doodle
- **MW (with KL/VB):** Take forward the development of a concept for a paper that analyses the benefits of radical technological developments in the clinical use of particles.