2022 ESTRO Physics Workshop: Science in Development

Joint DREAM (dose-response, experiment, analysis, modelling): a physics and radiobiology workshop

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Chairs: Heidi Lyng, Markus Alber, Mark Jackson, Laure Marignol and Ludwig Dubois

The first physics and radiobiology workshop aimed to foster not only communication, but also respective awareness and appreciation among modellers and experimentalists in the field of radiobiological modelling for radiation oncology. Thirty physicists and biologists met for a two-day workshop in Lisbon in October 2022 to discuss the current status of the field, identify the main challenges and develop strategies for implementing recommendations.

The workshop covered three sessions, each initiated by a keynote presentation from an invited speaker, followed by pitches from workshop participants. In the session on *defining the role of modelling in translational radiobiology*, Ivan Richter Vogelius (Copenhagen University Hospital, Denmark) provided a critical view of the current challenges and approaches for modelling. In the session on *artificial intelligence (AI) for radiobiology & dose-response modelling,* Issam El Naqa (Moffitt Cancer Center, USA) gave an extensive overview of the possible uses of AI and machine learning (ML) in this field. In the session on *calculation, interpretation and clinical implication of dose-modifying factors*, Conchita Vens (University of Glasgow, UK) discussed the obstacles in the way of translation of biological findings on dose-modifying factors into the clinic. The final part of the workshop consisted of three debates, for which all participants were split randomly into two opposing teams, either in favour of or against three statements: *if physicists were more rigorous with their models, biologists would embrace them; AI will boost quantitative radiobiology;* and *radiosensitivity can be reliably quantified.*

Figure 1: *Participants in the Joint DREAM physics and radiobiology workshop*

All sessions concluded with vivid, controversial discussions that not only revealed several overarching challenges in the field, but maybe more importantly, produced new impulses to seek solutions. A number of key vision statements could be formulated; these are explained below.

The unmet need for data

The predictive power of clinical models is limited mainly by data quality and quantity, and the statistically required patient numbers are seldom achieved in practice. With the emergence of new therapy options and combinations thereof, increasingly complex models are required, and these demand even larger amounts of data. Improving the standards for clinical data collection should be envisaged, but cooperative approaches between institutions will be increasingly necessary to overcome the data sparsity.

The robustness of preclinical experimental studies must be improved; often only snapshots, such as single doses and time points, are taken, so there is a risk that complex dynamics are missed.

Challenges for modelling

Clinical decision-making and trial designs demand well-validated, robust models. A shift of priority from the creation of new models to the validation of existing models should be encouraged.

The notion of complexity is central to radiobiological modelling. Awareness of its importance should be raised by experimentalists (who should consider which model simplifications are appropriate and which are not) and by modellers (who should consider why concepts such as parsimony are essential in model design).

Applicability of machine learning

Currently, there are two main areas in which ML is used in radiobiology: high-throughput data processing and data-driven outcome modelling. In general, models should be published in a way (optimally in combination with the training data) that enables comprehension and future validation. The appropriateness of ML-based models for different situations must be defined more clearly than it is now. While ML may be applied in descriptive modelling, hypothesis-driven, parsimonious modelling approaches might be preferable to create predictions and hypotheses. Before ML-based predictive models are implemented clinically, concerns regarding their interpretability and validation must be addressed, particularly since prospective studies are currently lacking.

Communication, collaboration, compromise

Successful collaborations between modellers and experimentalists are a cornerstone to bring radiobiological findings into the clinic. To ensure this success, both sides must appreciate the importance and difficulty of the other's work, be aware of mutual needs and be open to compromise. Collaborations should be well planned and intended to have long lifespans to encourage depth of understanding.

Conclusion

Based on the results of the workshop, the participants have agreed to write a vision statement that discusses the current most pressing requirements for the field and that proposes solutions and steps to encourage interaction. As a guideline and inspiration, it will also highlight successful engagements between the communities. A repository of resources for data analysis in radiobiology is a possible additional outcome. Overall, the concept of a joint physics and radiobiology workshop proved highly successful and should be repeated, possibly with a more specific focus next time.

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