protocols under experimental conditions. Our laboratory is developing an in vivo radiobiology research platform using the small animal radiotherapy research platform (SARRP, Xstrahl Life Sciences) as a central enabling technology to perform translational studies focussing on biologically optimised radiotherapy, nanoparticle theranostics and novel combination treatments. A major challenge now facing investigators is how to correctly apply the technology to accurately model clinical scenarios in relevant small animal models so that it can be exploited to its full potential in driving translational studies with outcomes likely to impact current standard of care in radiation oncology.

An overview of the current state-of-the-art in preclinical radiotherapy will be presented including recent developments such as integration of bioluminescence imaging, preclinical 4-D CBCT and Monte Carlo based dose calculation methods. Examples of innovative preclinical studies will be highlighted along with experience from our own laboratory from commissioning to experimental design and important considerations for the successful execution of hypothesis-driven investigations using small animal radiotherapy.

Despite certain challenges, small animal radiotherapy has much potential to bridge the translational gap between basic radiobiology and radiotherapy. As the technology develops and investigators gain experience as multidisciplinary scientists, pre-clinical studies that increasingly replicate the clinical scenario will drive new approaches in radiobiology that should ultimately translate to human health gains.

SP-0505 Radiation biology studies with a small animal irradiator: results from the Research Programme at Johns Hopkins University

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Although advances with in-vitro cancer cell culture models have occurred recently, in vivo tumor models are still crucial for the study of novel radiation treatments. This is particularly important for radiation combination approaches that target tumor cell non-autonomous anti-cancer pathways such as the tumor microenvironment or the immune system. In addition, more sophisticated animal studies with radiation are now possible with the advent of technologies that integrate treatment planning, imaging, and radiation delivery capabilities such as with the small-animal radiation platform (SARRP; Fig 1).

Clinical research faces many problems, of which the availability of pre-clinical models that predict the human situation is one of the most important. Pre-clinical tumour models are being used for decades in many cases with the assumption that they are predictive for what will later happen in humans. As such, the use of pre-clinical, mostly mouse, models may limit the exposure of inactive and or toxic treatments in patients. Although there is no doubt that pre-clinical models have been crucial to understand better molecular and other characteristics of carcinogenesis, growth and metastases and were the basis of many currently used cancer therapies, they still have considerable shortcomings. Classical mouse models use tumour cell lines that have been grown in vitro for many years and hence may have altered characteristics compared to de novo tumours. These tumour cells are then implanted subcutaneously in mice and tend to grow rapidly and thus do not mimic the much slower doubling times of most human cancers. This faster tumour growth may lead to a higher sensitivity for most chemotherapy drugs and hence erroneous conclusions. Moreover, in some situations, ectopic (out of the normal place) subcutaneously implanted tumours — still a standard methodology — may respond differently to treatment compared to tumours grown in an orthotopic site, i.e. in their organ or tissue of origin, such as breast cancers in mammary fat pads. The latter may correspond more to the human situation. Moreover, metastases frequently show other responses than primary tumours in patients, and it is only recently that these effects can be mimicked in genetically engineered mouse models. Tumour bearing mice are often treated with drugs at levels, or with pharmacokinetics, that are not relevant to humans. Furthermore, nearly all pre-clinical models have not used tumours that were pre-exposed to another therapy, whereas in many phase I and phase II clinical trials only patients that show tumor progression after one or more systemic treatments are included. With the huge interest in immune therapy, the use of humanised mice has gained even more attention than before. However, these models still face problems with remaining mouse innate immunity and weak human innate and adaptive immunity. Even the best models suffer from the development of wasting disease in highly engrafted humanized mice and poorly developed lymph nodes and germinal centres. It is also unclear if the cell trafficking resembles that of humans. At present, no single mouse models mimics perfectly the human situation. However, models that use injected tumour cells in the organ from which they are derived and which form metastases in organs that are similar to the human situation may be the most appropriate for they bear a micro-environment that resembles that of humans.

SP-0506 How do we select meaningful pre-clinical models for studies in radiation biology?

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Furthermore the kidneys filtered continuously thus there will be a marked difference in filling of the bladder with a rate dependant on the hydration status of the patient during radiotherapy delivery. Other factors may also be crucial such as bladder capacity and function as well as disease extent if it is bladder cancer. Therefore the variability of the bladder size and shape is an important consideration for any pelvic radiotherapy. Many investigators have reported on the marked difference in filling of the bladder with variation in bladder size that may range up to 20 mm on different scanning times during a course of fractionated radiotherapy. For primary bladder radiotherapy, identification of the disease extent remains important as both the target and tissue of tolerance is the bladder itself. This can also impact on the manner in which the bladder fills in 3D and be distorted by invasive bladder disease. It can be difficult to maintain daily consistency of the 3D shape and size thus there are several methods developed to deal with this including treatment with either an empty or comfortably full bladder to initiating adaptive planning and image guided delivery methods. Fiducials have been used to better target the main disease for either boosting disease or to incorporate focal therapy strategies. These methods can also permit organ avoidance if the bladder is an OAR and it is critical to minimise dose to it due to poor bladder function and other clinical factors. If the bladder is not the target then it can perform a useful function with intended filling prior to radiotherapy in order to displace other pelvic organs such as the bowel from irradiation such as with treatment of the pelvic nodes. Thus patient and disease related factors will need to be carefully assessed for each case. All these methods including their rationale and effectiveness will be discussed for both situations of the bladder as a target and as an OAR.

SP-0508
An evaluation of GoldAnchor intraprostatic fiducial marker stability during radiotherapy
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Background: Implantation of fiducial markers for IGRT (Image Guided Radiation Therapy) of prostate cancer patients increases the treatment accuracy by prostate localization using two orthogonal X-rays images. However the precision of the treatment depends on the stability of the fiducial marker. The aim of this study was to evaluate the migration of fiducial markers during the whole radiotherapy of prostate cancer patients.

Material and methods: An analysis of the intraprostatic fiducials migration during the treatment planning was done on a group of 45 patients on the basis on fusion of kV CBCT (performed during the first week of the treatment) and planning CT. The value of migration during the course of radiotherapy was done on a group of 20 patients treated within IGRT protocol on the basis on the fusion of kV CBCTs, performed weekly. The migration was defined as a shift between central points of markers, measured in three axis.

Results: The average values of the GoldAnchor™ migration during the treatment planning were: 1.1 mm (SD=0.9 mm) in the superior-inferior (SI) direction, 0.5 mm (SD=0.6 mm) in the left-right (LR) direction and 1.1 mm (SD=1.2 mm) in the anterior-posterior (AP) direction. The mean value of the vector of shifts was 1.9 mm (SD=1.3 mm). The average values of the GoldAnchor™ migration during the course of radiotherapy were: 0.1 mm (SD=0.2 mm) in the superior-inferior (SI) direction, 0.1 mm (SD=0.3 mm) in the left-right (LR) direction and 0.2 mm (SD=0.4 mm) in the anterior-posterior (AP) direction. The mean value of the vector of shifts during the treatment was 0.3 mm (SD=0.5 mm).

Conclusions: The analysis of the collected data showed that the marker shifts during the treatment planning seems to have no clinical significance and probably are related to the inaccuracy of the fusion of kV CBCT and planning CT. Position of the marker shifts during the whole course of radiotherapy. Therefore, IGRT based on GoldAnchor™ markers is safe and effective method of prostate cancer patient positioning.

SP-0509
Validation of a prostate cancer decision aid tool for shared decision making
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Purpose: To comply a decision aid tool with the criteria of the International Patient Decision Aid Standards (IPDAS), it is mandatory to follow a systematic and iterative approach to; (a) understand patient’s and clinicians decisional needs, (b) create prototypical tools, (c) evaluate these prototypes with patients and clinicians and (d) use these results to improve the tool. We developed and validated a web-based decision aid (DA) for shared decision making in prostate cancer patients using this approach.

Methods: A prototype of the tool was designed based on the input of an interdisciplinary group. Its clarity and acceptability was tested using a mixed method (interview and technology acceptance questionnaire; 5-Likert scale). The evaluation was performed with physicians (N=19) and patients (N=16). Professionals from 5 academic and private hospitals (urologists, radiotherapists, specialized nurses and family doctors) gave their perspective about the patients’ decisional needs and validated the information about the treatment options, complications and outcomes. The included patients were treated with either external beam radiotherapy, brachytherapy or prostatectomy. Patients who choose not to be treated (active surveillance) were also included. The decisional needs were evaluated during an interview. Afterwards the patients’ were guided through the DA and asked to fill in a questionnaire to check the comprehensibility of the tool. A second group of patients (N=8) was included to assess the e-learning effect of the DA and to check if patients were able to use the DA alone (without coaching).

Results: The results were considered to create a new version of the DA. Physicians mentioned the need of information about basic anatomy, contraindications, hospital specific figures, and psychological support. Patients reported that the