Teaching Lecture: Technology assessment

SP-0001
Technology assessment
D. Verellen[1]
[1]*Universitair Ziekenhuis Brussel, Radiotherapy, Brussels, Belgium*

Radiation therapy is a highly technology driven discipline, and as treatments become more complex and automated, safe implementation and quality assurance become less intuitive. Moreover, the discipline seems to face a dichotomous situation in that on one hand there is a tendency towards truly individualized treatments adapted to patient specific characteristics, short or long term variations in anatomy and delivered dose, that require flexible interventions and optimizations. These individualized treatments call for dedicated QA/QC programs. On the other hand the automatization in delineation and treatment planning in combination with the need to optimize workflows, drive development towards template driven, almost "app-like" solutions. The latter, seems to facilitate workflows and QA/QC procedures in that a strong standardization reduces the need for detailed verification. In fact, commercial solutions are being offered as "plug-and-play" with limited user interaction and QA/QC, almost ignoring the department's responsibilities towards patient safety and quality. Mix the previous with rapid succession of upgrades and updates, and it becomes clear that the assessment and QA of technology (still) requires constant attention and vigilance. Special care should be given to the workflow and how the individual components are integrated and mutually influence each other in this constantly evolving and increasingly complex situation. The presentation will also focus on the discussion between "one shoe fits all" solutions versus the need for dedicated technology. Are these decisions driven by clinical relevance or a "me-too" argumentation? Finally, some comments will be given comparing mono-vendor and multi-vendor situations.

Teaching Lecture: CRISPR/CAS technology: from cells to mice to stem cell therapy

SP-0002
CRISPR/Cas9 technology: from cells to mice to stem cell therapy
H. Te Riele[1], T. Harmsen[1], H. Van de Vrugt[1], J. Riepsaame[1]
[1]*Netherlands Cancer Institute/Antoni van Leeuwenhoek Hospital, Division of Biological Stress Response, Amsterdam, The Netherlands*

Protocols to efficiently generate small genomic sequence alterations in a targeted fashion are of great value to fundamental and clinical applications. We are particularly interested in developing protocols to correct the genetic defects underlying bone marrow failure in Fanconi anemia patients.
The most promising protocols for targeted correction or deletion of small mutations in terms of efficiency and facility make use of site-specific nucleases designed to generate a DNA double-strand break (DSB) in the genomic DNA closely located to the site to be modified. The *Streptococcus pyogenes* derived RNA-guided nuclease Cas9 combines strong and site-specific endonuclease activity with unprecedented design simplicity. By exploiting the endogenous error-free homology-directed repair (HDR) pathway that makes use of sequence homology, repair of the DSB can be accompanied by the introduction of specific base-pair alterations. When a double- or single-stranded DNA template is offered, the HDR reaction copies subtle sequence alterations present in the template sequence effectuating their introduction into the genomic DNA. For introduction of small alterations, short chemically synthesized single-stranded DNA oligonucleotides comprising 80-120 nucleotides are highly effective. We have optimized the protocol for single base-pair substitution in the genome of mouse embryonic stem (ES) cells by oligonucleotide-templated HDR of a CRISPR/Cas9-generated break, achieving precise introduction of a planned modification in 50% of the recovered cells. Furthermore, we studied the influence of the cell's DNA mismatch repair system on the efficiency of gene modification.
Fanconi anemia (FA) is a recessive heritable disorder characterized by skeletal abnormalities, progressive anemia and cancer predisposition. The disease is caused by bi-allelic defects in any of 17 genes, designated *FANCA*, *B*, *C*, etc. When a matching donor is available, bone marrow failure can often be treated by hematopoietic stem cell transplantation. Also, bone marrow transplantation from a non-matching donor can be offered, however, this is often associated with severe complications. An alternative strategy to re-establish a functional hematopoietic system may be the functional correction of the FA defect in the patient's own cells. Ideally, the defect is restored in the patient's own hematopoietic stem cells (HSC), which can subsequently be used to reconstitute the entire hematopoietic system. For FA patients with insufficient bone marrow cellularity, the FA defect may first be corrected in patient-derived primary fibroblasts. The corrected fibroblasts subsequently need to be reprogrammed into HSCs, most likely requiring the generation of induced pluripotent stem cells (iPSCs). As a first step towards this approach, we demonstrated that CRISPR/Cas9 genome editing can effectively be exploited to repair a deleterious mutation in *Fancf* and restore the FA pathway in cultured mouse ES cells and fibroblasts.
The next step is to use this protocol to correct the *Fancf* mutation in mouse-derived hematopoietic stem cells (HSC) and iPSCs. Gene-edited HSCs will subsequently be transplanted into lethally-irradiated recipient mice to determine their potential to drive long-term hematopoiesis. These preclinical studies are aimed to pave the way for the clinical development of CRISPR/Cas9-mediated gene correction protocols to restore FA gene defects and relieve bone marrow failure in Fanconi anemia patients.

Teaching Lecture: Partial Breast Irradiation: who, when and how?

SP-0003
Partial Breast Irradiation: who, when and how?
C. Coles[1]
[1]*Addenbrooke's Hospital, Oncology Centre University of Cambridge, Cambridge, United Kingdom*

This lecture will explore the rationale for partial breast irradiation and then discuss the results from randomised trials to date. These will include intra-operative radiotherapy, brachytherapy and external beam radiotherapy. There is considerable heterogeneity between these techniques in terms of target volume, dose and fractionation and possible consequences from these differences will be considered. Appropriate patient selection for partial breast irradiation and treatment outside clinical trials will also be discussed.

Teaching Lecture: New tools to reduce toxicity in pelvic radiation

SP-0004
New tools to reduce toxicity in pelvic radiation
I. Joye[1,2], K. Haustermans[1,2]
[1]*KU Leuven - University of Leuven, Department of Oncology, Leuven, Belgium*
[2]*University Hospitals Leuven, Department of Radiation Oncology, Leuven, Belgium*

Radiotherapy plays an important role in the treatment of pelvic tumors. The advances in patients' prognosis come at