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Biomechanics Based Microfluidic Biochip for the Label-free Isolation and Retrieval of Circulating Tumour Cells

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Immunomagnetic separation methodologies are currently the gold standard for circulating tumour cells (CTCs) isolation but face various drawbacks such as complex sample preparation and biomarker specificity. We developed a label-free biomechanics based microfluidic biochip that is capable of physically isolating and retrieving rare viable CTCs from cancer patient's blood. The principle is simple and makes use of the fact that cancer cells have biomechanical properties that are significantly different from that of blood cells. The key innovation lies in the unique crescent-shape microstructures which form the cell traps within the biochip. Instead of using biomarkers, these cell traps gently 'filters' CTCs from other blood components based on the biomechanical property differences between red blood cells, white blood cells and CTCs. Following this, the CTCs caught in these traps can then be retrieved in their wholly intact and viable state. Here, no sample pre-preparation of whole blood and antibodies is required. Blood collected in an EDTA tube can be processed straightaway in this biochip. Clinical blood samples from metastatic patients further verifies the applicability of the technique. Also, results from clinical tests showed that not all CTCs isolated were tested positive for EpCAM or CK. In fact, the CTCs were observed to be heterogeneous not only in terms of morphology such as cell size but also expression of EpCAM or CK. Significant number of CTCs where found to be EpCAM(−) or CK(−), CD45(−) but DAPI(+). This indicates that there are subpopulations of CTCs that warrants further investigation.

Society Session (Sun, 25 Sep, 16:45−18:15)
European Society for Therapeutic Radiology and Oncology (ESTRO)

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The Challenge of Tumour Heterogeneity

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Important advances in clinical care have been made through the development and implementation of standardized, evidenced based, treatment protocols in a variety of human diseases including cancer. Implicit in such standardization is an assumption that the nature of the disease amongst different individuals is similar, and that patients have equal probabilities of benefiting from the treatment in question. For cancer therapy in general, and radiation therapy in particular, this assumption holds only to a first approximation, as several known biological variables that influence treatment response vary significantly amongst patients. For radiotherapy, these include differences in proliferation, hypoxic fraction, and the intrinsic radiosensitivity of the tumour cells in question. Importantly, these biological phenotypes differ significantly both amongst patients and within tumours themselves. These two levels of heterogeneity represent both a significant challenge to treat patients effectively and also an opportunity for delivery of more personalized medicine. Understanding the genetic basis for this heterogeneity is assisting in the development of such personalize approaches to treatment. I will discuss our efforts to both understand the mechanisms that contribute to hypoxia tolerance in tumours and the genetic basis for these differences amongst tumours.

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Emmanuel van der Schueren Lecture − Intraoperative Radiotherapy in Multidisciplinary Oncology: Results and Innovations

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Intraoperative radiotherapy (IORT) is a multidisciplinar cancer treatment technique developd to improve the therapeutic-index of the combination of surgery and radiotherapy through the optimization of irradiation precision and the promotion of normal tissue tolerance (physical protection of non-cancer involved adjacent mobile organs and structures structures. IORT is a real-time vision guided and surgically supported (intra-pathology, normal tissue displacement, post-IORT reconstructive procedures). IORT as a dose-component (boost) for dose-escalation strategies has reported local control rates over 95% In adjuvant or high-risk post-resection cancer models (locally advanced primary rectal cancer, soft tissue sarcomas, breast cancer, etc.), over 70% in resection involved margin status (pelvic recurrences, oligotopic metastasis, etc.) and over 50% in unresected cancer patients categories (pancreatic cancer model). IORT is investigated as the sole component of irradiation (in the range of 20−22 Gy) in prospective non-inferiority randomized trials for early breast cancer with preliminary favourable results. Recent clinical innovations in IORT included the development of trials with IORT component and hypofractionated external radiotherapy, the incorporation of IORT to laparoscopic cancer surgery and the systematic evaluation of in-vivo dosimetry. Technical innovations are the development of miniaturized radiation devices specifically designed for intra-surgical use including high energy electrons or low X-rays source, together with treatment planning systems including virtual simulation, surgical navigation and dosimetric distribution estimations features. Surgeons, Radiation Oncologists and Medical Physicists will be guided by treatment planning systems in the decision-making process with an integrated multidisciplinary team-approach vision. IORT scientists and experts institutions have actively reported technical developments, clinical results and innovative projects. In the decade 1997–2007, 694 Pubmed indexed publications were available with accumulative impact factor over 1.300,000. An update up to May 2010, identifies 104 (277,856 I.F.) new additions. IORT belongs to the present multidisciplinary healthcare science imperative challenges to promote efficient human cancer control and improve patient quality of life.

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Radiation Oncology as a Clinical Specialty in a Multidisciplinary Environment: QUO VADIS?

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The incidence of cancer continues to increase throughout the world. Over the past century Radiation Oncology has solidified the basic foundations developed by the outstanding pioneers in our Specialty, it has established itself as a critical element, along with Surgery, Medical Oncology and other Specialties, in the multidisciplinary care of patients with cancer and it has evolved into a complex, clinically and technologically challenged medical discipline. Exciting developments in genetics and molecular biology/chemistry enhance the capability of Oncologists to more accurately classify the pathological features, behavior and prognostic implications of the cancer cells and the immunological mechanisms in the patients that may destroy them. Better understanding of radiobiological and physics principles have greatly contributed to te refinements in Radiation Oncology. There have been substantial advances in the ability of the Radiation Oncologist to evaluate our patients and the extent of their tumours, largely thanks to the advances in medical imaging, including MRI, PET and other modalities. Computational developments, imaging and sophisticated treatment planning algorithms have substantially contributed to the precision in treatment planning of radiation therapy, both with external beam and brachytherapy, leading to dose optimization, even in irregularly shaped target volumes, which has allowed dose escalation while preserving surrounding organs at risk in numerous anatomical sites. I envision cloud computing amplifying capacity and efficiency in radiation treatment planning and delivery, facilitating real time image-guided and adaptive radiation therapy. In the future new devices will have more refined imaging modalities with better anatomical and metabolic detail and they will incorporate more functional capabilities for dose delivered verification. The increasing use of combined modality therapy with cytotoxic or biologically targeted agents hormones, etc has enhanced the radiation effects in normal tissues and the probability of sequelea that may compromise quality of life of the patients. In the future it will be mandatory for Radiation Oncologists, Biologists and Physicists to continue basic science investigations to better understand the interaction of radiation with DNA and other molecular components of cancer and normal cells, to optimize the application of radiations to the treatment of patients with cancer. Nanotechnology is a most promising field, with potential applications in equipment design, specifically targeted anticancer drugs and agents to protect normal tissues from the effects of radiation. Radiation Oncologists must continue to foster and actively participate in pre-clinical research and in prospective clinical trials, such as those designed by ESTRO and RTOG and other Cooperative Groups, to maintain the scientific leadership that will ensure the active participation in the multidisciplinary care of the patients with cancer. Due to the complexity and increased possibility of errors in treatment planning or delivery of radiation, it is mandatory now and in the future to reinforce Quality Assurance and Continuing Quality Improvement Programs, to ensure the accurate treatment and safeguard the safety of our patients. Economic considerations play a most important role in everyday activities and the practice of Radiation Oncology is not an exception. We are motivated to use new technologies not only because of their marvels and