Conclusions: Individualized oncology will *revolutionize* health care providers: it will increase the complexity of health care but not necessarily increase the costs and it will improve the therapeutic ratio of our treatments through a better use of the existing knowledge. We anticipate that Decision Support Systems will.be the cornerstone of this revolution. Voxel Control/Complication Probability will give new opportunities to modern high precision radiation oncology. It will allow sculpting radiation dose alone or combined with drugs by taking advantage of tumour and normal tissue heterogeneity. In short, *both intra and interpatient heterogeneity give* new opportunities to improve our treatments

16 INVITED

Educating RTTS – a European adventure

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Background: The word education comes from the Latin *e-ducere* to lead out. Socrates saw education as drawing out what was already within the student. Education is a collaborative enabling process between the teacher and the student to stimulate a continuously enquiring mind. Essentially we fail if our students do not ultimately know or are not able to do and achieve more than we have.
Education should be an equaliser bringing professional freedom and autonomy. The education level of RTTs impacts on professional practice, multidisciplinary relationships and ultimately the preparation and delivery of optimum treatment to our patients. The theme of this presentation is on the efforts that have been made to improve education in order to enable RTTs to achieve autonomy and greater professionalism.
Education programmes for RTTs vary very significantly across the world, ranging from no specific education to an honours degree. This variation is also reflected in the lack of a unified title with as many as 50 different titles for this professional group. The variation in title has many implications for education and practice and results in a lack of recognition of the RTT internationally.
Over a twenty year period, I have developed the radiation therapy honours BSc programme in Trinity College Dublin and been involved in education initiatives such as the European Core Curriculum for RTTs, organising biannual conferences in conjunction with the main ESTRO Conference and the Physics meeting, developing and facilitating short courses and the final, and most exciting to date, the Train the Trainers project.
Train the Trainers: Twenty three participants, representing eight countries, were accepted onto the Train the Trainers project. The participants spent one week in Vienna in August 2008 where they were assisted by the teaching faculty to prepare an outline of a short course on a subject of their choice to deliver to a local audience of RTTs in their own country. Issues relating to the practical organisation of the short course were also considered. Each group committed to delivering three short courses over a two year period and to consider how the topic chosen could then be integrated into their national education programme.
Seven of the participating countries succeeded in preparing and delivering a short course. The topics covered a wide range of areas relevant to the local situation. Several of the countries attended each others courses and are making plans to share further short courses in the future. A feedback session is scheduled for August 2009 when each group will share their experience and discuss how they will now proceed.
During this presentation I will describe my experiences both nationally and internationally in raising the education level and professional profile of RTTs and how this work might be continued in the future.

17 Emmanuel van der Schueren Award

PET-CT imaging in radiation oncology

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Positron emission tomography (PET) with fluorodeoxyglucose (FDG) is a useful imaging tool in the management of cancer patients. The potential gains of integrated PETCT imaging are progressively being recognized. FDG-PET is able to measure and visualize metabolic changes in cancer cells. This feature results in the ability to distinguish viable tumor from scar tissue, in the detection of tumor foci at an earlier stage than possible by conventional anatomic imaging and in the measurement of alterations in tumor metabolism, indicative of tumor response to therapy. PET provides biological tumor information complementary to anatomical imaging by CT or MRI. Integrated PET-CT has found its way into clinical practice and FDG-PET is being introduced for staging, detection of recurrences, radiation treatment planning and therapy response monitoring and prediction. In addition to FDG, other PET tracers are available for imaging specific biological tumor characteristics involved in radiation resistance, such as hypoxia and proliferation.
Notwithstanding the potential of PET-CT, a critical appraisal of the current clinical state-of-the-art and the experimental application of this novel modality is necessary to allow timely implementation of clinical trials in daily patient care, but also to avoid overutilization.

18 INVITED

Combining EGFR inhibitors with radiation

P. Harari[1]. [1]*University of Wisconsin, Dept of Human Oncology, Madison, USA*

The incorporation of molecular targeted therapies into modern cancer treatment regimens is relatively recent, reflecting several decades of molecular biology coming to fruition in the form of new anti-cancer drugs. The EGFR inhibitors are one class of highly promising agents in this arena. Thousands of cancer patients are currently receiving EGFR inhibitors and a broad series of clinical trials that incorporate these agents are in progress. Combining EGFR inhibitors with radiation has shown particular promise for patients with cancers of the H&N. Indeed, the first Phase III clinical trial to identify a survival advantage when combining a molecular targeting agent (anti-EGFR) with radiation emerged fairly recently in H&N cancer (NEJM 354:567−78, 2006).
Accompanying the promising clinical development of EGFR inhibitors in cancer therapy are several challenges. For example, molecular strategies of EGFR inhibition demonstrate major tumor regression in approximately 10−20% of cancer patients. However, many tumors do not show response to EGFR inhibition and some responders eventually manifest resistance to treatment. The underlying mechanisms of intrinsic and acquired resistance to EGFR inhibitors remain largely unexplored. Although the toxicity profiles for EGFR inhibitors do appear milder than that of conventional cytotoxic chemotherapy agents, the unique toxicities of EGFR agents are nonetheless important to recognize and treat appropriately. Finally, many of the new molecular targeted therapies (including EGFR inhibitors) are remarkably expensive. This high cost reflects the manner in which new drugs are discovered, developed and promoted in the current era, and this feature carries implications regarding the broad availability of these new cancer drugs in the future.
The logical integration of basic science with clinical research will further define the spectrum of benefits and toxicities associated with each new cancer therapy. This is certainly true for the combination of EGFR inhibitors with radiation (or chemoradiation); an area that is advancing, but still at a relatively early stage of overall development. As with all treatment advances, it is valuable for oncologists to remain actively engaged in evaluating the rational and judicious application of each new treatment approach.

19 INVITED

Identification of gene variants and gene expression profiles predicting long term adverse side effects of radiation treatment in breast cancer patients

A.L. Børresen-Dale[1]. [1]*The Norwegian Radium Hospital, Department of Genetics, Oslo, Norway*

In breast cancer (BC) patients with regional lymph node metastases loco-regional radiotherapy (RT) is an established adjuvant treatment. Improved detection and early diagnosis are likely to increase the importance of loco-regional control and hence the success of RT. Radiation oncologists have for a long time known that individuals respond differently to radiation. In addition to the variation in tumour response, some patients show severe side effects when exposed to small doses of radiation, while others tolerate larger doses without much complication. To be able to protect radiation sensitive (RS) patients against the adverse side effects of RT, identification of such patients before initiating therapy is needed. RT kills cells unselectively and irradiation of normal tissue may cause severe side effects that appear at different time points. Acute side effects may emerge during or shortly after a course of RT and these early reactions condition for many BC survivors, leading to a reduction in quality of life. To explore the underlying cause of radiation sensitivity we have taken several approaches. Germline variation in genes like *ATM, CHK2*, *BRCA1/2* and *GSTs* are studied in several series like the WECARE (Women's Environment Cancer and Radiation Exposure) involving 700 cases with contra lateral BC and 1400 matched unilateral BC with detailed information about radiation treatment, and in a series of 245 receiving a high dose of radiation compared to a control series receiving standard dose, both extensively evaluated for radiation damage 10 – 15 years after treatment. These studies are ongoing and updated results will be reported.
Gene expression profiling of fibroblasts exposed to radiation form BC patients previously treated with IR and evaluated for response and morbidity identified a set of genes involved in extracellular matrix to predict fibrosis.

Fatigue is one of the most frequent complaints among BC survivors receiving RT. To explore whether biological processes underlying persistent fatigue can affect gene expression of blood cells, genome-wide expression analyses were performed on whole blood samples from BC survivors classified as chronic fatigued (CF) 2−6 years after diagnosis. Non-fatigued survivors served as controls. Several gene sets involved in plasma- and B cell pathways differed between the CF and the non-fatigued, suggesting that a dysregulation in these pathways is associated with CF and that a B cell mediated inflammatory process might underlie fatigue. The chronic fatigued also had a higher level of leucocytes, lymphocytes and neutrophils compared with the non-fatigued, thus further indicating that an activation of the immune system plays a role in the biology of CF in BC survivors.
With the above studies we hope to identify gene variants and gene expression profiles that predict long term adverse side effects of RT in BC patients that will shed light of the different mechanisms involved in order to develop preventive strategies.

References

Bernstein et al BCR 2004.
Olsen et al BJC 2005.
Rødningen et al Radiot. Onc 2005.
Langholz et al IJC. 2006.
Helland et al. Radiot. Onc. 2006.
Edvardsen et al IJ Rad. Onc Biol. Phys. 2007.
Landmark, et al Radiot Onc 2007.
Edvardsen et al. Radiat Oncol. 2007.
Rødningen et al Radiot. Onc. 2008.
Concannon et al. Cancer Res. 2008.
Landmark-Høyvik et al Pharmacogenomics 2009.

Society session (Mon, 21 Sep, 11:00−13:00)
SIOPE session

20 SIOPE Award

Multisystem Langerhans Cell Histiocytosis: progress in clinical management despite controversial biology

H.G. Gadner[1]. [1]*St. Anna Children's Hospital, Vienna, Austria*

More than a century after the first description of Langerhans cell histiocytosis (LCH), it is still an intriguing disease with a broad variety of presentation and enigmatic biology. Therefore, the management concepts over time have been changed according to the view on the nature of the disease process. At the beginning of the 20th century, LCH was believed to be of infectious or metabolic origin and starting with the unifying concept of "histiocytosis X" in 1953, it was considered a malignant disease. Hence, staging systems derived from other malignancies (e.g. lymphomas) were used. Some multi-institutional studies conducted in the USA between the 1950 s and 1970 s contributed to a better description of the disease variables and elaboration of treatment schedules. However, in the 1980 s, with the belief that LCH was a reactive rather than malignant process, the disease lost scientific interest and LCH fell into the category of "orphan diseases". Two prospective clinical trials in the early 1980 s (DAL-HX 83 and AIEOP-CNR-HX 83), both applying stratified systemic chemotherapy promptly after diagnosis, showed improvement in prognosis and reduced reactivation rates. These studies form the basis for the international trials (LCH-I, LCH-II, and LCH-III), conducted by the Histiocyte Society since the early 1990 s, after worldwide acceptance of uniform diagnostic criteria and disease stratification (single system (SS) vs multisystem (MS) LCH with/without risk organ (RO) involvement). The randomized LCH-I trial (1991–1995) compared vinblastine and etoposide in the treatment of patients with MS-LCH, and confirmed an equivalent efficacy of both drugs. Another important finding of LCH-I was that response to initial therapy is a reliable prognostic factor allowing for risk stratification and respectively tailored treatment intensity. The LCH-II trial (1996–2001) built upon the results of LCH-I, was a randomized phase-III trial for patients with risk MS-LCH (RO involvement: liver, spleen, haematopoetic system and/or lungs). In this study the effectiveness of 6 months therapy with the combination of oral prednisone, vinblastine and mercaptopurin, which has been established as a standard therapy for LCH, was compared to the same combination with the addition of etoposide. Overall, there was similar outcome in both therapy arms regarding early response, 5-year survival probability, disease reactivation frequency, and permanent consequences. Considering only risk patients the addition of etoposide showed significantly better results regarding speed of initial response and survival, thus, emphasizing the need of a more intensive approach in children with RO and resistant disease. In the LCH-III study (2001–2008) two randomized trials were incorporated. In the risk group the 12 months of steroids and vinblastine (standard arm) was compared to standard arm plus methotrexate, as an attempt for further improvement of survival and reactivation-free rate. The preliminary results of the LCH-III study do not show advantage of the addition of methotrexate. However, the overall survival of 85% at 2 years is the best result ever achieved in risk patients. In the low-risk group (no RO) the standard arm was randomly given for 6 or 12 months. The longer treatment arm showed a significant benefit in prevention of disease reactivation. Evolving knowledge of the disease biology will hopefully open new approaches for even more effective disease control in the near future.

Advocacy Session (Mon, 21 Sep, 13:30−15:00)
Informed cancer patients receive better treatment and care

21 INVITED

Surviving childhood cancers 'Informed cancer patients receive better treatment and care'

A. Brownsdon[1], C. Hails[1]. [1]*Independant, Cancer Survivorship, London, United Kingdom*

Rapid progress in the successful treatment of childhood cancers over the last 40 years has led to a new, ever expanding, cohort of childhood cancer survivors. For the authors, surviving childhood cancer has been an immensely positive opportunity and their experiences have led them both to pursue careers in healthcare. Whilst recognising that they are not unusual in this respect, the authors acknowledge that other survivors have not been so fortunate and may have suffered from late side effects of their treatments and/or encountered difficulties adjusting to a life that is no longer defined by cancer itself – whether this be at school, at work or in society.
Newly diagnosed patients can access information from a range of sources (including doctors and other healthcare professionals, the internet, cancer charities and other survivors) but the authors consider whether it is possible to truly be an 'informed cancer patient' when there is still so much that is unknown about the disease itself, treatments and their effects – both short-term and long-term.
They then focus on survivors as a source of information for patients, clinicians, and policy-makers, drawing on examples of a survivor mentoring programme, survivor representation on the British Childhood Cancer Survivor Study Steering Group and survivor representation on the Children and Young People's Workstream of the National Cancer Survivorship Initiative in the UK.
The authors share their experiences of being involved with the International Childhood Cancer Survivors' Network and how information is shared between patients, survivors, parents and clinicians globally. An international perspective has alerted them to the fact that they approach this subject from the privileged position of growing up in a country with a National Health Service and recognise that in many countries it is the family's economic circumstances that dictate the level of treatment and care the child receives, rather than their level of knowledge.
Finally, the authors discuss whether it should be the case that informed cancer patients receive better treatment and care. They conclude that all patients should be treated equally and receive the best available treatments based on clinical needs rather than on their access to information or financial circumstances.

22 INVITED

Talking with patients about expensive and unavailable new cancer drugs

L. Fallowfield[1]. [1]*University of Sussex, Oncology, Brighton East Sussex, United Kingdom*

Some very exciting developments have been made in the past decade which mean that more patients are being cured of cancer and/or living longer with meaningful remissions of their disease. The research community continue to make important discoveries that permit treatment to be tailored more precisely to an individual patient with these novel targeted therapies. Unfortunately many of these new treatments are extremely expensive and the healthcare budgets of most of the developed world are facing an impossible situation of having finite resources but infinite demands for the latest drugs. Arguments as to who should fund these ever expanding costs are heart-breaking for patients and their relatives who are desperate for access to the best available treatments. The media and popular press often fuel the debate in unhelpful ways by portraying benefits too optimistically. For healthcare professionals who practice in state-funded healthcare environments, sensitive discussions that should be happening about prognosis, supportive care and other end-of-life care