**12** INVITED

**New imaging in cancer clinical trials**

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There is increasing use of novel imaging methods in oncology trials. Aims include the development of early indicators of clinical response, proof of principle or pharmacodynamics studies. Methodology involves contrast enhanced or radio isotope techniques such as DCE-MRI or FDG PET where the physiological properties of the probe determine information available, and modality sensitive studies such as diffusion weighted or spectroscopy MRI.
In order to carry out these studies the investigator must have expert help to address important considerations. Imaging tests must be practical, affordable, ethical and relevant. Analysis of the results of tests requires quality control and knowledge of inter and intra patient reproducibility. Data must be analyzed and handled according to the same constraints as all clinical trials data. These issues are particularly difficult when setting up multi-centre trials.
This talk reviews the various imaging approaches available, potential problems and possible strategies.

**13** INVITED

**A clinical development paradigm for cancer immunotherapies: novel endpoints**

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The effect of cancer immunotherapies is on the immune system and not directly on the tumor. The kinetics of immunotherapy is characterized by a cellular immune response followed by potential changes in tumor burden or patient survival. To adequately investigate immunotherapies in clinical trials, a new development paradigm including reconsideration of established endpoints addressing this biology is needed. Between 2004 and 2009 several initiatives across the cancer immunotherapy community were facilitated by the Cancer Vaccine Consortium of the Cancer Research Institute (CVC-CRI). They systematically evolved an immunotherapy-focused clinical development paradigm and proposed to re-define trial endpoints. On that basis, analysis of several large data sets generated throughout the immunotherapy community support three novel endpoint proposals: (1) Results from T-cell immune response assays are highly variable and often non-reproducible. Harmonization of assays can minimize this variability and support to establish cellular immune response as a biomarker and test it for clinical surrogacy. (2) Immunotherapy induces novel patterns of anti-tumor response not captured by WHO or RECIST criteria. New immune-related Response Criteria (irRC) were defined which more comprehensively capture all response patterns. (3) Survival curves in randomized immunotherapy trials can show a delayed separation, which can impact study results. Altered statistical models are needed to describe the hazard ratios as a function of time, and differentiate them before and after separation of curves to improve planning of Phase 3 trials. Taken together, these recommendations may improve our tools for cancer immunotherapy investigations.

## *Advocacy session* (Mon, 21 Sep, 11:00−13:00)
## Advocacy in practice

**14** INVITED

**Patient groups − meeting the challenge of sustainable funding**

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Advocating for a cause has been part of peoples behaviour for centuries. This is what is entailed in moving away from the personal experience to advocating for a cause that is much broader and in using this experience to effect change.
Where patient rights are concerned individulas have organised themselves into groups in order to raise their voices, to have dignity and equality in key issues, and to finally take part in the decision making process.
Patient groups have had to become more and more organised and structured, voices have to be well informed and well educated, in order to maintain the strength in collective action.Patient groups have in many cases moved away from being seen as threatening to professional and scientific organisations to being equal partners.Health care professionals have been under pressure to recognise and follow these changes, while patient groups have had to rise to a different set of challenges.
The changing voice of patient advocacy has led to the voices leading to political change. It has led to legislations that have safeguarded patient rights, that have led to the aims and goals placed by cancer advocacy movements to be translated into governmental policies and decisions, it has led to lobbying at national and other levels, thus placing the foundations for all that has been achieved in the revolution of cancer diagnosis, prevention and treatments.
Patient rights have been cemented by Charters and even acquired legal status so that they are not left up to individuals.
As science has progressed, issues have become more complicated, and patient groups have had to become more diverse and work together not only with professionals, but also with media, politicians and industry. This has in its turn created new realities for the processes needed by patient groups and placed demands on their needs for funding.
Issues related to the source of funding, the necessary transparency and the diversity have been in the forefront of many discussions over the last few years.
The issue of sustainable funding and the relationship of patient groups to industry has been a source of debate and often of controversy.
Patient advocacy is never static, it is a changing journey that aims at impacting positively on all those affected by a disease. The credibility of this voice will determine its effectiveness and strength- and this is what is required when any patient group is brought before the issues related to funding.

## *Society session* (Mon, 21 Sep, 11:00−13:00)
## The European Society for Therapeutic Radiology and Oncology (ESTRO)

**15** Klaas Breur Award

**From patients to Voxels: Individualized oncology and "Voxel control/complication probability"**

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*Inter*patient heterogeneity: the need of a "Decision Support System" to facilitate tailored oncology.
Over the past decades we have witnessed an unprecedented increase in our basic understanding of cancer at molecular level, experienced a huge improvement in medical technology and have access to an ever increasing amount of data on cancer. As a consequence, modern medical diagnostic systems confront doctors with a flood of digital and molecular data.as well as a greater than ever amount of therapeutic options. "One size fits all" and "more for all" are no longer an option. Doctors are notorious for being bad at predicting the outcome of various treatments. Therefore doctors need a "*Decision Support System"* (DSS) which not only integrates all diagnostic information and therapeutic options but also, in the future, will take into account the wishes of the patient. Such programmes will make it possible for medical professionals to propose tailored made treatment plans to patients. We anticipate that DSS will become compulsory as Treatment Planning Systems are presently for complex Radiation. An example of first generation DSS, namely validated nomograms or gene signatures in solid cancer will be presented (Valdagni *et al.* IJROBP 08; Dehing *et al.* IJROBP 08−09; Starmans *et al.* BJC 08; van Stiphout *et al.).* The development of DSS has already made an impact on the way we carry out clinical research.
*Intra*patient heterogeneity: the need of "Voxel Maps & "Uncertainty Based Planning"
It is now clear that both tumours and many dose-limiting organs are not homogeneous structures with respect to their biology, environment and radiation sensitivity. Importantly, new imaging modalities are enabling the possibility of both assessing this heterogeneity and incorporating it into therapeutic decisions.
We hypothesise that future processes of radiation oncology will be based no longer on margins, but on at least *two probability maps* and verification of the delivered dose. (1) *Imaging-based Voxel Control Probability (VCP)* or *Parametric Response Map* which consists of fused images before and during treatment that will lead to information on the probability of relapse per voxel (Laprie *et al.* IJROBP 2008; Galban *et al.* Nature Med 09; Aerts *et al.;* Petit *et al*. R&O 2009). This allows optimization of the tumour dose distribution to minimize the probability on residual disease. (2) *Voxel dose probability,* describes the chance that a voxel has of actually receiving a certain dose given a planned dose distribution. This is needed to make the multi-dose level treatment plan more robust when not using margins. (3) Verification of the actual cumulative dose delivered using *3D in vivo dosimetry* (van Elmpt *et al.* IJROBP 09). Further refinements of this approach are possible by taking into account the effect of *systemic treatments* and other *clinical, biological and genetic factors* present in the above mentioned DSS.