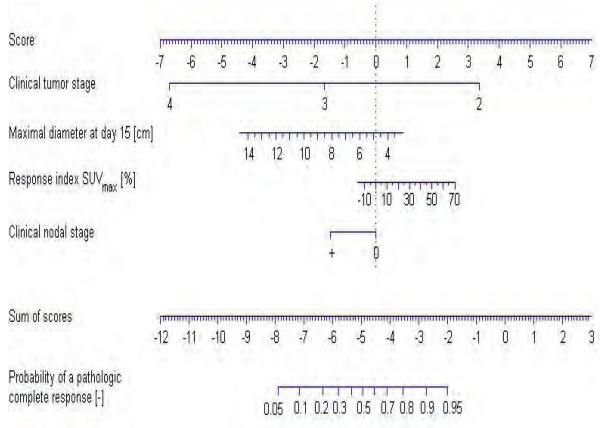
increasing the quality of life. A prospective trial to test decision making with the model versus a controlled group with standard treatment is the next step towards implementation of a decision support system for rectal cancer.



SYMPOSIUM: FUTURE RADIOTHERAPY CLINICAL TRIALS: SALT, PAPRIKA AND MOLECULAR SIGNATURES AND RT

SP-0423
The implications & challenges for clinical trial design involving radiotherapy
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Modern radiotherapy research is built on well validated biological and physical hypotheses which will be tested in the clinical trial. The trial design must enable the investigator to obtain a clear answer to the primary trial objective, through clear enunciation of the primary hypothesis, the endpoint to be measured and an appropriate statistical design to enable the hypothesis to be evaluated in a way which is reliable. The extreme heterogeneity of cancer is leading some investigators to think that conventional clinical trial methodology is outmoded and that fundamentally different approaches are required. Individualisation of therapy on the basis of tumour genotype, imaging or both is portrayed as the goal of modern cancer therapy. Individualisation of radiotherapy occurs in every case through the treatment planning process and within clinical trials this must be undertaken within the constraints of a prospectively optimised and agreed radiotherapy treatment protocol and commensurate RT quality assurance process to be delivered before and during the trial. Similarly biomarker or imaging based treatment allocation or randomisation requires the use of rigorous technical delivery of the assay or scan and an agreed method of interpretation of the outcome. In phase 1 drug radiation trials, delays while waiting for assessment of radiotherapy toxicity risk making such studies too slow and relatively early dose escalation and 'flip-flop'design evaluating two novel agents in alternating dose escalation cohorts is an efficient design. Multi-stage trial designs can speed up the phase II/III evaluation of novel therapies, while enabling early termination for futility. The SCOPE-1 trial of the addition of cetuximab to chemoradiotherapy for oesophageal cancer is an example. Prospective molecular sstratification of patients for intervention trials relevant to the specific abnormalities in their tumour can be designed but require extensive collaboration and large numbers. Such designs are coming into stratified drug trials such as the FOCUS4 study in metastatic colorectal cancer and the applicability to radiotherapy studies will be discussed.

SP-0424
Fractionation protocols in the age of targeted therapies ñ should we change and how?
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Abstract not received

SP-0425
Molecular imaging as biomarker in future clinical trials: The proof of the pudding is in the eating
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Integration of molecular imaging techniques into therapy selection strategies and radiation treatment planning can serve several purposes. First, pretreatment assessments can steer decisions about radiotherapy modifications or combinations with other modalities. Second, biology-based objective functions can be introduced to the radiation treatment planning process by co-registration of functional imaging with planning CT-scans. Thus, customized heterogeneous dose distributions can be generated with escalating doses to tumor areas where radiotherapy resistance mechanisms are most prevalent. Third, monitoring of temporal and spatial variations in these radiotherapy resistance mechanisms early during the treatment can discriminate responders from non-responders. With such information available shortly after the start of the treatment, modifications can be implemented or the radiation treatment plan can be adapted tailing the biological response pattern.
Currently, these strategies are in various phases of clinical testing, mostly in single-center studies but more and more also in multi-center set-up. Ultimately, this should result in availability for routine clinical practice requiring stable production and accessibility of tracers, reproducibilty and standardization of imaging and analysis methods and general availability of knowledge and expertise. Small studies employing adaptive radiotherapy based on functional dynamics and early response mechanisms demonstrate promising results. This approach is closest to large scale clinical testing with good prospects for success.

SYMPOSIUM: METHODS FOR QUALITY MANAGEMENT

SP-0426
Quality management for contemporary and emerging RT technologies
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The definition of quality in radiation therapy largely remains poorly defined, understood and often confused with the issues of safety. While safety and quality are on many levels inseparable, there is a clear distinction and there can be delivery of safe treatments according to physician prescription in radiation therapy which are of insufficient quality to meet the treatment goals. High quality clinical operations can be defined as those which minimize variations and uncertainty in patient treatments and result in consistent outcomes. In radiation therapy, treatment consists of multiple components (consultation, treatment selection, immobilization, imaging for planning, contouring, planning, etc.). Relatively large variation and uncertainty in any one of these steps contribute to the overall degradation of treatment quality. The degradation of quality results in uncertainty in patient outcomes. Figure 1 a) shows an example distribution of patient treatments. On one end of the spectrum is overdose of critical structures, in middle are the majority of patient treatments which result in clinical benefit without unexpected side effects,and on the other side of the spectrum is under dose of target volumes. The over dose and under dose is clearly bad, but the two regions between clinical benefit and over dose and under dose, respectively, have clinical uncertainty. Patients falling in these uncertainty regions may or may not have clinical complications or poor tumor control. Patients falling in extreme over or under dose regions are typically infrequent and these are extreme cases that typically are widely publicized. However, it is unclear how many patients fall in the uncertainty regions and potentially have compromised outcomes. It is important to note that the outcomes in the uncertainty region are often considered as expected and accepted treatment outcomes, though possibly avoidable.