improvement program which is fully embraced by the European CanCer Organisation (ECCO). Initially, the focus will be on colorectal cancer. In the first period of 2 years the registration will make use of currently existing audit systems for colorectal cancer as in Norway, Sweden, Denmark, the United Kingdom, the Netherlands and Belgium, and start a benchmarking process. The national audit coordinators will provide access to their national databases and will form a multidisciplinary Steering Committee. The second period starts after the development of the European registration system. The data will be continuously used for benchmarking and internal feedback among participants. Afterwards, this experience will be used to extend the audit to other solid malignancies such as breast, gastric and oesophageal cancer. Data and experiences with colorectal audits will be discussed but indicate vast improvements of outcome.
Conclusion: Recent developments in quality assurance in surgical oncology have resulted in improvements that have a greater impact on survival than that of any of the adjuvant therapies currently under study. A European audit could advance future improvements and spread these to every cancer patient in Europe. The ECCO has recognised the importance of quality assurance and has created a framework to develop a European audit. As such, ECCO has established a strong, multidisciplinary organisation with a commitment to improve cancer care in Europe. All information about this project can be found on the website:
www.canceraudit.eu. Persons involved in the treatment of colorectal cancer and interested in joining or contributing to this European colorectal audit ECCO project can contact the authors at anytime.

137 INVITED

Quality Assurance of Radiotherapy

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Objectives: In Radiation Oncology, QA systems are based on audits, which can be either internal or external to the Institution. Internal audits can, for instance, track intra-fraction and/or inter-fraction variations (e.g., variations in prostate position in function of rectum and bladder volumes). In this latter case, actions will be taken to match simulation and treatment settings, and random or systematic differences will be reported and recorded by the staff of the treatment unit. External audits can be national or international, performed on site or at QA review centers. They can be institutionally oriented, for instance, to check the accuracy of the beam calibration performed by the center. They can also be performed in the framework of prospective clinical studies, and conducted by experts of cooperative groups.
Material: In this case, the parameters requested and/or deviations investigated by the QA provider use to encompass: a) a definition of GTV, CTVs and PTVs; and b) an identification of isodose distributions underdosing GTVs, under/overdosing PTVs and/or overdosing critical organs such as, for instance in head and neck oncology, the spinal cord, brain stem, optic nerves and chiasm, etc.
Methods: At least two quality systems are essentially proposed to the investigators: the “dummy-run” and the “individual case review”, which were developed within EORTC. These procedures investigate both the compliance of individual institutions to the protocol guidelines and treatment accuracy. As regards the former one, in the very early phase of a trial activation, participating centers are given a number of reconstructed slices of the anatomical region of interest, including target volume contours, and asked to generate the irradiation plan them according to the protocol guidelines. As regards the latter one, it is based on the collection of images and data specific to individual cases treated in the framework of a given protocol. It generally includes diagnostic CT-scans, MRI and/or PET scans, planning CT-scans, treatment plans with dose distribution in target volumes. It is performed at the completion of the treatment (final review), but can also be “interventional” and scheduled at the very early phase of a trial activation.
Results: The clinical outcome of QA programs conducted in the framework of trials is not always easy to quantitate in terms of efficacy results or impact on quality of life. Examples of direct relationships between poor compliance to protocol guidelines and poor clinical results will be presented, especially as regards regimens combining radiation and drugs.
Conclusions: Among the main messages retrieved from a recent past, it can be shown that poor quality irradiation invalidates the scientific rationale of randomized trials of combined modality treatment, and centres enrolling only a few patients are the largest source of quality problems. Therefore sites involved in clinical research need to be rigorously credentialed prior to enrolling patients and interventional review should ideally be done before RT commences. At community level, doing well what we already know is more important than seeking incremental gains through new treatments.

Scientific Symposium (Sun, 25 Sep, 09:00−11:00)
Novel Oncoproteomic Technology

138 INVITED

Label-Free Mass Spectrometry-Based Proteomics for Biomarker Discovery and Validation in Tissues and Biofluids

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Background: Colorectal cancer (CRC) is the second leading cause of cancer death in the Western world. Detection of CRC at an early stage of disease is associated with a much better prognosis for the patient, and is a realistic approach to reduce CRC mortality rates. Several randomised trials have shown that FOBT screening, ie detection of blood-derived haem in feces, reduces CRC mortality by ~16%. Nevertheless, the FOBT test performance is relatively poor, and it is commonly recognized that sensitivity and specificity of non-invasive CRC screening tests need to be improved, for which novel biomarkers are urgently needed.
Label-free mass spectrometry-based proteomics in (pre)-clinical samples and tumour proximal biofluids is emerging as a powerful, versatile approach for discovery of tissue-derived biomarkers with close association to the disease.
Aim: The aim of our studies is to identify novel protein biomarkers that can be used for development of a stool-based, blood-based, or molecular imaging-based screening test for early diagnosis of CRC.
Approach: Proteomics targeted to “biomarker-rich” compartments (proximal fluids, cell surface, nucleus) using a label-free GeLC-MS/MS workflow and spectral counting for protein quantitation. We have shown that this workflow is reproducible and outperforms other commonly used workflows in terms of the total number of identified proteins and the total number of reproducible identified proteins (Piersma et al., J.Proteome Res. 2010; Albrethsen et al., Mol. Cell. Prot., 2010).
Results: We have analyzed three different CRC model systems: 1) Proximal fluids of a mouse model for human sporadic CRC, which lacks variation due to genetic heterogeneity and allows to compare tumour-to matched control-samples; 2) Secretomes, exosomes and cell surface fractions of a panel of five human CRC cell lines; and 3) Proximal fluids and nuclear fractions of human colon adenoma and carcinoma tissues combined with patient-matched control tissues.
By combining proteome profiles of proximal fluids obtained from different CRC model systems we succeeded to identify tens of candidate biomarkers for stool-based or blood-based early detection of CRC. By combining cell surface proteomics with transcriptomics of adenomas and carcinomas we identified candidate biomarkers for molecular imaging of adenoma-to-carcinoma progression.
Outlook: We are currently validating these candidate biomarkers by IHC, ELISA and Selective Reaction Monitoring mass spectrometry using large series of clinical samples, in order to compose a *panel of biomarkers* with high sensitivity and specificity for CRC early detection and screening.
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High Resolution Mass Spectrometry-Based Proteomics for Metabolism and Cancer Research

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Recent Breakthroughs in mass spectrometry based proteomics enable the detection adn quantification of thousands of proteins in complex mixtures. In addition, these methodes allow for the quantification for global analysis of changes of posttranslational modifications, such as phosphorylation. The basic principles of the methodology will be discussed using examples of metablism and cancer research.

140 INVITED

Clinical Proteomics in the Early Detection of Breast Cancer

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The completion of the human genome as well as the explosion of novel technologies within genomics, proteomics and functional genomics promise