

NRAS oncogenes. Many other molecular abnormalities have been reported in other genes such as PI3K, PTEN, AKT1, MDM2, APC, HER2, KDR, MET, CTNNB1, ATM, BRAF, AKT1 and more recently ALK as well as FGFR1. Of note FGFR1 amplification has been reported in up to 20% of squamous cell carcinoma and 5% of adenocarcinomas.

Beyond the now classical oncogene-drivers represented by EGFR mutation and ALK translocation, many other molecular abnormalities could be used for selection of specific therapies such as amplification of HER2 and FGFR1; or activating mutations of HER2, HER3, HER4, FGFR2, KDR... Nevertheless the correlations between the presence of such abnormalities and clinical response are still not firmly documented, although some interesting case reports have been reported. The table below provides a summary of specific alterations, their frequencies and their potential corresponding molecular targeted interventions. DNA repair markers are also potential predictors of standard anti-cancer therapies (ERCC1, MSH2, BRCA1, PARP).

Scientific Symposium (Sun, 25 Sep, 14:45–16:45) Improved Pain Control Through a Collaborative Approach Between Oncology, Pain and Palliative Care Specialists

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INVITED

How to Improve Cancer Pain Control Through European Guidelines for Opioid Treatment and Cancer Pain Diagnosis

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The principle for optimal cancer pain control with primary focus on the use of opioids was published as a second edition by WHO in 1996. The analgesic ladder concept, in which the choice of analgesics is determined by the severity of the pain, is the central idea behind the opioid guidelines. Despite the global impact of the WHO guidelines, 50% of cancer patients with pain are not adequately treated. Barriers to optimal pain control may be linked to 1) insufficient knowledge about the pathophysiology of cancer pain, 2) inferior assessment and classification of cancer pain, 3) sub-optimal treatment, and 4) inadequate implementation of evidence-based knowledge into clinical practice. An updated version of the European Association for Palliative Care (EAPC) guidelines were published in 2001. The guidelines have been criticized for the non-systematic approach in the development, and incomplete review of available literature. Therefore a rigorous evidence-based methodology and a wide international development process was initiated, and in 2011 the Evidence-based Guidelines for the use of Opioid Analgesics in the Treatment of Cancer Pain: the 2011 EAPC Recommendations are emerging. The present version of the EAPC guidelines contain substantial novelties, also in content. One relevant change regards the content of recommendation 2, which modifies the original role of oral morphine as a first step-three opioid. This recommendation values the available evidence from studies with other opioids (hydromorphone and oxycodone), but also acknowledges the lack of evidence supporting the description of first choice for any of these drugs.

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Chemotherapy Including Modern Targeted Therapies to Prevent and to Treat Cancer Pain

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Despite decades of research the evidence that palliative chemotherapy prevents or relieves cancer pain is very limited. Although it is widely held that tumour shrinkage is generally associated with relief of pain there is a profound paucity of data concerning the analgesic benefits of cytotoxic chemotherapy and biological therapies. Direct evidence of analgesic benefit is restricted to a very small number of trials mainly in pancreatic cancer and prostate cancer. Bone modifying agents such as bisphosphonates and denosumab have, overall, shown only limited analgesic effects and there major benefits have been related to the prevention of painful bone related events. This presentation will review existing data and propose that pain

related data be collected in a more systematic manner in clinical trials, particularly among patients with advanced cancers.

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INVITED

What is the Place for an Effect of Surgery to Prevent And/or to Treat Cancer Pain

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The paradox when considering surgery to prevent/treat cancer pain is of course that surgery itself causes pain. Post-operative pain usually subsides within 1–2 weeks but sometimes can be longlasting which has been emphasized in a review by Perkins and Kehlet. They concluded that long lasting post-operative pain has an incidence of up to 50% or more in studies of breast surgery, thoracotomy, and amputations.

Besides pain, surgery is inevitably connected with other types of morbidity and even mortality. This makes the decision when to make use of surgery indeed challenging. A conscious calculation of pros and cons has to conclude that the advantages dominate. If the realistic goal of care is cure, radical surgery is the main option in many cancer diseases. The meticulous use of skin incisions and tissue friendly dissection techniques that minimizes the risk of nerve injuries are known to decrease the frequency of post-operative neuropathic pain.

In a palliative context performance status, length of survival, chance of effect, risk of complications, time to recovery, and patient's acceptance of the proposed surgical intervention are factors to be included in the decision making process. When estimated survival prognosis is less than a couple of months large surgery is, in principle, contraindicated. Minimal invasive techniques may still be justifiable if the non-surgical treatment alternatives have failed or are likely to have little or no effect.

Stabilizing orthopedic surgery for painful skeletal metastases, stenting, by-passing or venting procedures for mechanical obstructions of bowel, bile or urinary tracts, limb amputation in selected cases of sarcoma or melanoma, neuroablative or neurostimulatory procedures, implantation of neuropharmacologic delivery systems are examples of surgical procedures that can increase pain relief. Meticulous patient selection and timing is of outmost importance to succeed.

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What is the Place and Effect of Radiotherapy and What is the Optimal Schedule for Cancer Pain

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The place for radiotherapy in cancer pain, is any situation where pain can be related to a mass effect or infiltration of a local tumour. The mechanism of pain may be complex and radiotherapy may affect not only the tumour bulk itself, causing extensive cell death but also the release of nociceptive cytokines and nerve conduction. It is therefore active both in visceral, musculoskeletal and neuropathic pain.

Pain relief after radiotherapy is generally good with both high response rates and durable response seen. As an example, metastatic bone pain will respond in 70 to 80% of patients with a durable response for many months often spanning the remaining life expectancy of the patient. Similar response is seen with bone related neuropathic pain, pain from non small cell lung cancer (NSCLC) and from progressive liver metastases.

The optimal schedule for cancer pain in the palliative setting is the lowest amount of radiotherapy which is compatible with efficacy. As a basic principle if this can be achieved with a single dose of radiation this will be the optimal schedule.

There is good level 1 evidence to support this policy in metastatic bone pain, neuropathic pain, and NSCLC. Short fractionated schedules delivering 5 to 10 treatments may be preferred in some settings, for example in brain metastases, where there may be impending spinal canal compression or pathological fracture from painful bone metastases and in NSCLC patients who have good performance status and limited metastatic disease.

In summary, radiotherapy is the most effective treatment for cancer pain in many settings where the mechanism of pain is due to direct tumour growth with 70% or so of patients having durable response from low dose treatment often requiring a single exposure of radiation.

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A Future Research Agenda to Improve Pain Control Through Collaborative Efforts

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Many of the cancer patients suffer from pain during their illness. Mostly the analgesia follows the WHO ladder approach. For severe pain we use

different opioids in different application forms. Luckily we have choice of different opioids with their advantages and disadvantages. But some problems of opioids are class effects or problems of the opioid system (opioid receptor). In this meaning, new opioids will only have a limited chance for further progresses in analgesia. So-called co-analgesics act mostly through the effect of, what has a more or less effect of sedation with it. New drugs has to take into account, that pain is multidimensional and has something to do with awareness, categorizing, and other learning effects of the brain, which are very different in our patients. This means, that a multidimensional approach of the pain is necessary. For this approach we have to understand, what the pathophysiology of the pain is, what the pain means for the patient and if the nervous system and the brain are already hyper alert or hypo alert. Only if we have understood this step, we can do a better and more individualised pain therapy.

For research that means, that we can't see the pain only as a illness of the nervous system on the basis of receptors, transmitters and nerve fibres. We have also to look after the functioning, the learning style, the coping mechanism, fear and other psychological and social reaction to know how to intervene best.

Scientific Symposium (Sun, 25 Sep, 14:45–16:45) The Role of Medical Technology in Building a Sustainable Cancer Care

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INVITED

How Medical Technologies and Pharmaceutical Industry Can Work Together

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Over the last five years, scientists and engineers at GE Global Research Center have been developing a new fluorescence microscopy-based method for multiplexed analysis of >30 proteins *in situ* in a single section of formalin fixed paraffin embedded tissue (FFPE). This provides high content fluorescent imaging at the single cell level and uniquely enables the simultaneous evaluation of multiple markers in multiple sub-cellular compartments, without destruction of the sample. By inclusion of epithelial, stromal cellular proteins in the multiplexed staining sequence, we have demonstrated subcellular protein expression, phosphorylation and co-localization in individual cells. Since multiple proteins are analyzed on the same tissue section, precious clinical sample is saved. Collaborating with pharma and clinical institutes has been an essential part of this work, and has ensured the validity of the technology, the needs of researchers are met and the end applications are clinically relevant. Over the last 4 years, we have been working with scientists at Eli Lilly to utilize the multiplexing technology to evaluate potential predictive and prognostic biomarkers as part of their drug discovery process. New insights have been gained into biomarker response in drug-treated xenografts and heterogeneity of biomarker expression prostate cancer. This collaboration could ultimately lead to new diagnostics for patient stratification and prediction of drug response.

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INVITED

Recent and Future Advances in Cancer Imaging

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Cancer care today involves millions of multi-modality imaging exams, including CT, MRI, PET/CT, SPECT, X-ray and Ultrasound. Advances in cancer imaging are driving new clinical standards in early detection, targeted therapy and assessment of treatment response. Early detection is being improved by advances in imaging resolution, soft tissue visualization and anatomical+functional detail. These advances also enable therapy targeting with millimeter precision, and targeting in the presence of anatomic motion and physiologic change. Quantitative measurements enable rapid assessment of treatment response and recurrence, driven by technological advances, validated software tools, and standardized clinical protocols. Future advances in cancer imaging will continue improve care across the cancer lifecycle.

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INVITED

IT Enabled Clinical Decision Support and Integration of Cancer Care-Role of EMR and Cancer Registries

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Background: Electronic Medical Record (EMR) systems dedicated specifically to the care of cancer patients are widely available and currently

in common use world-wide. For Radiation Oncology, they are an absolute necessity for treatment delivery. As these systems have evolved, they have become both more sophisticated and have been increasingly integrated into the workflow throughout the cancer care continuum. For example, they have not only been equipped with provisions to support control of complex external devices such as linear accelerators, but also with interfaces to exchange data with allied information systems, features to enhance treatment safety, and direct connections to cancer registries. Ultimately, these types of capabilities are expected to facilitate continuous improvements in cancer care and treatment outcomes.

Using the Elekta EMR (called MOSAIQ) as an example, we will demonstrate the ability of such systems to support a new Electronic Health Record paradigm that promotes this advanced clinical decision support and facilitates the integration of cancer care programs.

Material and Methods: Architecturally, MOSAIQ is deployed in a way that allows users in a Medical Oncology facility to readily share data and information with Radiation Oncology users managing a common cohort of patients, leading to highly integrated and coordinated care. Data elements collected represent a rich superset of Cancer Registry data.

A pilot study of the use of this system as the foundation for establishment of a real-time radiation oncology data registry was mounted in the USA in 2009. The aggregate is composed of de-identified demographic, treatment and follow-up data routinely collected in the course of patient care, and automatically collected and uploaded from each participant's EMR to a central data warehouse on a monthly basis. This system is intended as a model that will be used for the establishment of a US Comparative Effectiveness Research registry on behalf of ASTRO's National Radiation Oncology Registry (NROR) program, and thus designed to be readily scaled in terms of numbers of facilities, number of data elements collected, and geographic locations.

In conjunction with these efforts, features are being incorporated inside MOSAIQ to support "intelligent" care delivery capabilities and permit, for example, the implementation of structured treatment protocols that can be modified to accommodate workflows specific to a locale. These protocols can be followed within and across centers, and can help coordinate and support care delivery in a consistent and structured manner.

Results: The MOSAIQ software is in use in approximately 60% of radiation oncology RO clinics in the US, with significantly increased utilization outside of the US, (37% and 54% growth in 2010 and 2009 respectively).

For the registry pilot program, approximately 50 demographic, treatment and follow-up data elements are collected. These data are core to patient care and routinely collected during treatment, and thus have required minimal additional burden on the part of participating facilities.

To date, a total of over 171,800 patient records have been aggregated over a course of approximately 1,576 automated de-identified data uploads from approximately 35 participating facilities. Data collection adherence for any particular element varies across the facilities, with some nearing 100% compliance and others ranging as low as 20%.

Efforts to enhance MOSAIQ for the purposes of improving data consistency and quality are being pursued. Hard coded safety-related interlock integrated into the software and incorporated into the work flow double as data quality enforcement tools, and a process being released will support development of customized alerts and interlocks and that will further enhance data quality.

Standard treatment protocols that support the management of patients in accordance with certified guidelines are incorporated into the system along with direct links to guideline agencies such as NCCN. Along with provisions to determine eligibility for clinical trials, these features provide a toolset that can be used to manage patients both on and off of clinical studies.

Conclusions: Electronic Medical Records systems used for Oncology care are amongst the most advanced available and in use today. Provisions to support treatment pathways, to enhance and enforce safety, to collect and aggregate data in near-real time, and to feed such data back into these systems to support decision making are among the current and near term features being incorporated into these systems. These programs will not only lead to safer, more efficient and effective care, but will also form the foundation for support of world-wide comparative effectiveness research (CER), guideline-directed care, and enhanced utility of device technology which should ultimately cascade to outcome improvements universally.

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INVITED

Molecular Diagnostics Role in Personalised Cancer Care

Abstract not received

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The Future of Radiation Therapy in Comprehensive Cancer Care

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Cancer is a very challenging condition and one of the fastest growing health challenges in the developed world. As cancer is not one but hundreds