a myriad of clinical responsibilities to the entire surgical team to promote positive patient outcomes.
This presentation will describe and discuss opportunities and issues for nurses who are new to, about to become involved with, or, who are already involved with robotic surgery; ***from handmaiden to right hand.***

39 INVITED

Health-Related Quality of Life as a Prognostic Factor in Patients With Oesophageal Cancer

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Background: Since treatment for oesophageal cancer is extensive and the long-term prognosis is poor, tools that can help predict the prognosis are warranted. The use of measures of health-related quality of life (HRQL) are becoming increasingly more common in clinical research, and accumulating evidence suggests that HRQL data can predict survival in oesophageal cancer patients.
Materials and Methods: The literature as available on PubMed was reviewed on this topic. Several cohort studies have been performed, some of which have been of population-based design. Results from randomised clinical trials with HRQL as a secondary outcome were reviewed also. The assessment of HRQL has mainly been based on the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30) together with the oesophageal-specific module (QLQ-OES18).
Results: Based on the available literature, where adjustment for potential confounding factors has been performed, poor global quality of life, poor physical and role function, fatigue and appetite loss before treatment appear to independently predict a worse chance of survival. HRQL measured after treatment may also be of prognostic value. When measured 3−6 months after oesophageal cancer surgery, poor global quality of life, physical function and social function and symptoms of fatigue, pain, dyspnoea, appetite loss, dysphagia and odynophagia are associated with shorter survival. Improvement in physical function within 6 months of surgery has been found to be associated with a better chance of survival while increased pain and fatigue is associated with worse survival.
Conclusions: Measures of HRQL might be of use in predicting survival in patients with oesophageal cancer. HRQL can be used in clinical practice to direct the need for investigations to detect recurrent disease, and in the planning of follow-up, supportive care and palliative treatments. However, more research is needed to clarify the role of HRQL as a prognostic tool in the clinical management of oesophageal cancer patients.

Special Session (Sat, 24 Sep, 14:15−15:15)
Late Toxicity Treatment of Head and Neck Cancer

40 INVITED

Biological Insights

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Despite relatively high survival rates, the quality of life of head and neck patients is severely compromised because of radiation-induced impairment of salivary gland function and consequential xerostomia (dry mouth syndrome). Although is some patients a recovery can be seen even up to 5 years after irradiation, mostly the damage is permanent. Similar late regeneration of the salivary glands has been show in rats after fractionated irradiation. From these preclinical experiments radiation-induced hyposalivation has been described in 4 distinct phases. The first phase (0−10 days) was characterised by a rapid decline in flow rate without changes in amylase secretion or acinar cell number. The second phase (10−60 days) consists of a decrease in amylase secretion and is paralleled by acinar cell loss. Flow rate, amylase secretion and acinar cell numbers do not change in the third phase (60–120 days). The fourth phase (120–240 days) is determined by a further deterioration of gland function but an increase in acinar cell number, albeit with poor tissue morphology. The most primitive tissue stem cells, residing in the excretory duct seem to be responsible for the late regeneration of the tissue. Indeed, the maintenance and repair of the tissue integrity are the primary roles of the tissue stem cell. Stimulation of stem/progenitors before or after irradiation with e.g. pilocarpine of KGF, results in enhanced regeneration which however does not always lasts. Therefore, for the normal tissue it is of eminent importance to spare the tissue stem cells. Recently, it became apparent that the tissues stem cells may not be evenly distributed over the tissue. Irradiation of a critical 7 volume % part of the parotid glands, suggested to contain the tissues stem cells, indeed resulted in more than a proportional damage as shown by the reduced saliva production, whereas the non-centrally orientated volume induced a lower than proportional level of damage. Next to the tissue stem cells, also the vasculature plays a prominent role in late tissue damage. Together with extensive fibrosis, prominent telangiectasia can be observed in the salivary glands late after irradiation. However, mobilisation of bone marrow derived mesenchymal cells and endothelial progenitor cells have been shown to be able to prevent late vascular damage in the mouse salivary gland. In conclusion, the tissue stem cells and the vasculature play a major role in late salivary gland damage. Here specific sparing of high stem cell density regions together with enhanced circulating endothelial progenitor cells may yield an enhanced recovery after irradiation and improved salivary gland function.

41 INVITED

Late Functional Outcome in Chemo-Radiation

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The last decade, major progress has been made in the treatment of head and neck squamous cell carcinoma (HNSCC). There is growing evidence that more aggressive treatment regimens, either the delivery of radiotherapy with concomitant chemotherapy or altered fractionation schedules, improve tumour control and survival. However, these new treatment regimens have come to the expense of radiation-induced side effects (RISD), such as swallowing dysfunction and xerostomia. As quality of life is particularly affected by RISD, prevention of this side effect may improve the therapeutic ratio of treatment for HNSCC. One of the ways to prevent RISD is to reduce the dose to the anatomical structures involved in swallowing, i.e. the swallowing organs at risk (SWOARs) and salivary glands.
At the department of Radiation Oncology of the University Medical Center, all patients with head and neck cancer undergoing curative radiotherapy are subjected to standard follow up program in which acute and late toxicity is prospectively and systematically assessed at fixed time points during and after radiotherapy. Currently, more than 800 patients have been entered in this program, which enables studies on the relationship between radiation dose distributions in several organs at risk (OARs) and late toxicity.
In our prospective cohort, we found that xerostomia is the most frequently reported grade $\geqslant$2 RSID. Since the introduction of IMRT, the prevalence of this side effect has been reduced significantly as compared to 3D-CRT without sparing of the parotid glands. Recent results of our preclinical studies indicate that further improvement may be achieved by specifically sparing certain sub volumes within the parotid glands.
Another important late side effect is swallowing dysfunction, which has a major impact on patient-rated quality of life. The results of our prospective study showed that the dose in specific anatomical structures, such as the dose to the pharyngeal constrictor muscles and the supraglottic area are the most important factors for late swallowing dysfunction. In addition, swallowing dysfunction more frequently occur among patients treated with chemoradiation. In silico planning comparative studies indicate that sparing these SWOARs may result in a reduction of the risk of this side effect. The first results of a prospective phase II study on swallowing-sparing IMRT look promising in this regard. These results will be presented.
Conclusion: Parotid sparing IMRT significantly reduces the risk on xerostomia. Further improvement may be expected from sparing specific sub volumes of the parotid glands and possibly by proton radiotherapy. Swallowing sparing IMRT is expected to result in a significant reduction of swallowing dysfunction after curative (chemo) radiation.

42 INVITED

Late Functional Outcome Surgery

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Today's main guidelines for treatment in HNSCC are still based on phase III-trials and comprehensive metaanalysis with excess of radiation or chemo radiation at the expense of surgical trials. As stated by Higgens and Wang (Higgens 2008), clinical recommendations for HNSCC treatment based on evidence are difficult due this disproportion of surgical and non-surgical trials. This conflict is triggered by the fact that instruments for evaluating best surgical practice are different from methodological standards in non surgical phase-II or -III trials (this is nicely considered by Higgens 2008). Late functional outcome after surgery is becoming more evident since late functional outcome after multimodality treatment has been augmented as issue in comparison of best treatment in head and neck squamous cell carcinoma (HNSCC). To address this problem, Lefebvre and Ang

(Lefebvre & Ang 2009) worked out a list of guidelines for better outcome-specification after organ preservation therapy, which should be used in further clinical trials. The paper introduced a new endpoint: "laryngo-esophageal dysfunction-free survival" and addressed the growing problem of lat dysphagia in larynx preservation programs. Due to this discussion, many surgeons come back to more surgical driven decision making since late toxicity outcome after surgery seems to be limited compared to current protocols of simultaneous chemoradiation. Standards in surgery of HNSCC are defined as state of the art tumour resection procedures and reconstruction, following consented resection criteria like clear margins (R0-resection). Also neck dissection is standardized (AJCC) and should be included into the tumour stage related surgical concept. Altogether, primary surgery in HNSCC and additional adjuvant treatment is generally recommended if R0 resection is possible. Regarding late functional outcome, instruments for objective comparison of results are lacking. Health related quality of life (EORTC) and International classification of function (ICF WHO) are relatively new tools for better evaluation of late functional outcome.

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Special Session (Sat, 24 Sep, 14:15−15:15)
Issues in Economic Evaluation of New Cancer Therapies

43 INVITED

Cancer Drug Costs − Forecast for Europe − Will the Cost Explode?

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We have seen a number of new cancer drugs being approved over the last 10−15 years. During the first part of this time period an average of 2−3 new drugs were approved each year and over the last years 8−10 drugs. This increase in available drugs is results of improved understanding of cancer biology that we have seen develop during the last three decades. These new treatment options have, however, come at a significant cost. Spending on cancer drugs has increase 5−6 fold, in some countries even more, over the last decade (www.comparatorreports.se). This should be put into the context of about 2−3 times increase in the total costs of cancer care seen in most European countries during the same period of time.
Will this increase in cost of cancer drugs continue and if so, will society be able to handle the costs of cancer care? First we must realize that much of the spending we see on cancer drugs relates to "mature" drugs, i.e. drugs that have been available for more than a decade. Many of these drugs have just gone off patent or will soon go off patent; the price of docetaxel, constituting about 8−10% of the cost for treatment of solid tumours in Sweden, decrease by >95% in just 2−3 months. We will most probably witness a similar cost reduction for the aromatase inhibitors, as all of them are likely to go off patent during 2011. As a majority of the top 20 selling cancer drugs will be generic in a couple of years, this will leave us with some budget available over the next 3−4 years.
We have also seen a number of drugs with similar mode of action (for example TKIs) being approved, resulting in substitution price competition rather than more patients being treated. This, at least temporary, situation will give us opportunity to improve the way we evaluate new cancer drugs and drug combinations, introducing HTA as a key part of the introduction process. We also have time to set up proper, population based, systems for monitoring the effects of new treatments in the "real" world. We can, in addition, continue to develop new innovative pricing models.
Meanwhile, we must also address the inequalities we have within Europe, with many countries in central/ eastern Europe (most of them new members of the EU) having a significantly lower access to up-to-date cancer care, including drugs. These inequalities may need political action on a central EU level. Our aim should be to bring new innovative, evidenced based, cost effective cancer treatment to all cancer patients in need across Europe.

44 INVITED

Methodological Issues in Economic Evaluation of New Cancer Therapies

Abstract not received

45 INVITED

Performance-Based Agreement − Theory to Practice- the Current Use in Oncology and Future Trend

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Health care systems are increasingly evaluated on performance and outcome, rather than for availability and use of resoruces. The background to this is the slow growth in health care expenditures and fiscal problems in most developed economies. Improvements in quality of care and outcome through a more cost-effective use of existing resources is the main option for development of the services. Relative effectiveness and cost-effectiveness are new criteria for decisions about adoption and use of new cancer drugs, which gives HTA and reimbursment bodies acting on behalf of payers, an increasing influence over therapeutic decisions.
A problem for decision makers is that there is limited information available for undertaking such evaluations before there is evidence from acual clnical use of the drugs. In addition, payers are concerned that expensive new drugs are used for the patients that can benefit most. The increasing use of coverage by evidence schemes and risk-sharing agreements between manufacturers and health authorities are responses to the above. In performance based agreements, the payment for the drug is dependent on the outcome or result of the intervention. The theoretical arguments for such arrangements are for the payers that it gives incentives for an efficient use of resources and access for patients, and for manufacturers that it may give a faster introuduction on the market.
Oncology drugs seems to dominate the among the performance-based agreements we know today. In Italy for example, 16 out of 18 risk sharing agreements until October 2010 relate to cancer drugs. However, it shold be noted that not all contracts are based on performance. Many risk sharing agreements include just a price discount, for example related to the number of cycles given. Most contracts in cancer use response as criteria for perfomance. The precise definition of "performance", or more often non-performance, is obviously of great importance for both parties of the agreement. But those criteria are seldom very explicit, carefully followed up, and openly discussed.
The trend is for an increasing number of performance based agreements in the future. So far private and public health insurers have mainly requested and paid for data on patient characteristics, but the new interest in comparative effectiveness research will likely result in payments are related to outcome. Public health care systems in Europe, usually organized as a payer-provider split, will increasingly look for conract that help them manage costs and outcome.

Special Session (Sat, 24 Sep, 14:15−15:15)
Too Little or Too Much Surgery for Melanoma

46 INVITED

For Sentinel Node Positive Patients − is Complete Lymph Node Resection Still the Standard of Care?

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Standard of care is defined as how reasonable and similarly qualified physicians would act under the same or similar circumstances. The largest study on what surgeons do in case of a tumour positive sentinel node concerns 2942 patients in the USA. Of these patients, 1470 were subjected to a completion node dissection (50.0%). The other 50.0% were spared a node dissection. Apparently, there is no standard of care. This is understandable because the only prospective randomized study addressing this important question is in progress. For now, the practicing surgeon has to rely on circumstantial evidence.
Completion node dissection reveals additional metastases in 11−20% of the patients. Half of these patients will develop distant metastases from which they will die irrespective of a node dissection. Another third can still be cured if the node dissection is deferred until the development of palpable nodal disease. So, the potential gain in survival is limited.
A watch and wait policy limits the node dissection to the minority of patients who do have metastases and spares the vast majority of individuals an unnecessary operation. The downside is that the disease may disseminate from the nodal basin to distant organs in the time before the first nodal metastasis becomes palpable.