skin, limbs, gynaecology and digestive surgery area, in which reconstruction was essential in obtaining a better oncological control and a better quality of life.

1061

How to do the sentinel node?

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It has been shown sufficiently that the sentinel node procedure (SNP) is -at least- equal to axillary lymph node dissection (ALND) or axillary nodal sampling to show or exclude axillary lymph node metastasis in the great majority of patients. Many experienced "teams" are able to identify the SN in the axilla in almost 100% (> 95%) of patients, and after backup axillary clearance the false-negative rate (missing the positive node) varies between 1-5%. In general, 30-40% of SN are tumour positive, and a further 40% of non-SN in the axilla contain metastases. Till date, it is not possible to predict a less then 10% chance of non-SN positivity if the SN is positive, even if primary cancers are small or SN contains only micrometastases. Therefore, if the SN is tumour positive, treatment of the axilla, either by ALND or by radiotherapy, is advised.

The SN-procedure may serve two aims:

Omitting axillary treatment (clearance) in patients who's axillary SN are tumour negative. If this is the main goal, different injection techniques (intratumoural, peritumoural, subareolar, intracutaneous, low versus high volumes) appear not to matter: all techniques will result in the identification of the SN in the axilla in the great majority of patients.

Lymphatic mapping. The identification of all tumour positive SN around the breast: in the axilla, intramammary, periclavicular and/or in the internal mammary chain nodes (IMC). If this purpose is aimed at, only parenchymal injection techniques (intratumoural, peritumoural) will drain the tracers to these sites. Some groups showed a 30% drainage to extra-axillary nodes (20% IMC), 80-85% retrieval rate and about 20% are tumour positive (5% the only positive node). Albeit that with this technique staging of the primary cancer is improved, it is unclear whether this will lead to important changes in treatment and consequently more or less toxicity and a better outcome.

What are to steps to be taken to achieve a high identification rate and a low false negative rate?

1. Start with a proper training course.
2. Go through a learning curve of at least 20 patients.
3. Work within a proper team (breast surgeon, nuclear medicine and pathologist).
4. Indication: unifocal invasive breast cancer, < 3-4 cm, clinically node negative.
5. Use preoperative ultrasound of the axilla and FNA-cytology.
6. Use the triple identification technique: lymphoscintigraphy, patent blue dye, intraoperative probe and palpation of the axillary content.
7. Use IHC with cytokeratins in the SN to reduce your false negative rate.
8. Maintain your experience by performing at least 5-6 cases a month.

Be careful in the following clinical situations (these indications are considered experimental):

- Multifocal invasive cancer.
- After large excisional biopsies.
- After upfront or neoadjuvant chemotherapy.
- In DCIS.

1062

Signal transduction therapy

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Over the past 20 years the molecular bases of numerous diseases have been discovered. The pathophysiologies of many of these diseases are frequently derived from aberrations in either **intra** cellular or **inter** cellular signaling pathways. This is particularly true of proliferative diseases such as cancers, leukemias, atherosclerosis, restenosis and psoriasis and of inflammatory diseases such as sepsis, rheumatoid arthritis, autoimmune diseases and tissue rejection. These findings have refocused medical research on seeking out new modalities for disease management. The new paradigm shift focuses on designing therapeutic modalities aimed at restoring normal signaling or bringing about the demise of the diseased cells without harming their normal neighboring cells. In the lecture we shall discuss this paradigm shift and cite the emerging therapies based on the new molecular understanding of signal transduction pathways.

1063

New directions in the treatment of mesothelioma

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The causative association between occupational exposure to asbestos and malignant mesothelioma has been identified in 1960.Taken into account a latency period of 20-50 years and a decline on workplace exposure in Europe after the 70ies it has been estimated that the incidence of mesothelima in Europe will double each year until about 2020. Over 80% of mesothelioma arise from the pleura, the reminder from the peritoneum, the pericardium, and the tunica vaginalis. Histologically, malignant mesothelioma is commonly classified into epithelial (60%), sarcomatoid or mixed type. For staging of pleural mesothelioma the TNM system is commonly used. Up to now, there has been no uniformly accepted standard therapy for pleural mesothelioma. The best-documented potentially curative approach to mesothelioma has been pleuropneumonectomy, followed by chemotherapy and radiotherapy (trimodality approach) in selected patinas with earlier stages of disease. The absence of mediastinal lymph node metastasis and the presence of the epithelial subtype are associated with a better prognisis. Several chemotherapeutic agents demonstrated activity against mesothelioma in phase II studies; these include doxorubicine, platinum compounds, vinorelbine, and the antimetabolites. Several recent studies phase II studies have documented good activity combining cisplatin/gemcitabine and oxaliplatin/raltirexed. A major step forward has been the only prospective randomized study in pleural mesothelioma comparing single agent cisplatin with the combination of cisplatin and premetrexed, which demonstrated superior survival for the combination therapy. In vitro, several signal transduction pathways have been identified to be of importance in mesothelioma, including EGF, TGFα, VEGF, PDGFβ, bcl-2/bcl-xL, survivin and trail. Promising preclinical results have been obtained with the EGFR tyrosine kinase inhibitor gefitinib, but the result of a recent phase II study have been disappointing. Full adjuvant chemotherapy after pleuropneumonectomy is not feasible in many patients. Based on the promising results of neoadjuvant chemotherapy in non-small cell lung cancer and the availability of combination chemotherapy with reasonable clinical activity such as cisplatin/gemcitabine, we initiated a multicenter study of three cycles of neoadjuvant chemotherapy followed by pleuropneumonectomy with or without radiotherapy to problem regions. Intermediate results will be presented.