(3) Isotope or blue dye are both: Many methods are described using different isotopes and different routes of administration. Which blue dye and which isotope and the timing and route of administration require further evaluation.

(4) Immunohistochemically positive nodes: The significance of immunohistochemically positive sentinel nodes is unknown. How we should manage these patients is unclear. The value of PCR positive sentinel nodes is even less clear.

(5) Internal mammary nodes: what to do with internal mammary nodes that light up on the lymphoscintigram remains uncertain. The prognostic significance and the value in excising these nodes may need to be re-evaluated in the sentinel node era.

(6) Credentialling for Surgeons: This remains a controversial issue for surgeons in practice.

Sentinel lymph node mapping has established itself as a valid technique in the management of breast cancer, however before it is acccepted as standard of care the aforementioned controversies need to be addressed.

1561

Sentinel node biopsy in melanoma. Is it worthwhile?

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Lymphatic mapping and sentinel node biopsy is one of the major developments in surgical oncology in this decade. This minimal invasive procedure allows for the identification of clinically occult lymph node metastases, avoiding needless extensive lymphadenectomy. In melanoma patients the technique of sentinel node biopsy is well cristallized, with an identification rate of the sentinel node in 99% of the cases. Reported false-negative basin recurrences, approaching 15% of expected node-positive basins in some series, however, is a matter of concern.

A clear advantage of sentinel node biopsy is that it allows for improved staging, now that the pathologist has the unique opportunity to focus his diagnostic tools on one node only, instead of on a whole dissection specimen. The clinical relevance of this pathological scrutinizing by serial sectioning, immunohistochemistry and the molecular staging technique of RT-PCR for tyrosinase mRNA, however, still has to be proven. The same applies to the intriguing supposition that earlier entry of lymph node positive melanoma patients into adjuvant regimens might be of benefit.

The most crucial question to be answered is, if a positive sentinel node biopsy with subsequent lymph node dissection improves regional tumour control and survival. This issue is at present addressed in a randomized study, initiated by the inventor of the method, D.L. Morton. The outcome of this trial will hopefully bring the long standing debate on the value of elective lymph node dissection to a conclusion. Until then sentinel node biopsy remains an experimental procedure.

1562

Early stage prostate cancer – Watchful waiting or radical treatment?

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The management of early prostate cancer has been described as the most controversial issue in contemporary oncology. Outcome data are simply too inadequate to allow the formulation of any scientifically wellfounded guideline for decisionmaking. As a corollary, conflicting recommendations have been issued and widely differing treatments used by various professional organizations. The best we can look for is an open debate about issues of a broad range: biological, clinical, ethical, economic, and others. We need to respect differences in opinion while walling for data from randomised, controlled trials.

The management of early stage prostate cancer need also be discussed and understood in the context of screening with prostate specific antigen. Such screening is not only likely to advance the time of diagnosis of cancers that would otherwise have surfaCed clinically at a more advanced stage, perhaps many years later; it may also entail overdiagnosis of histopathologically malignant lesions with limited or no potential to progress to mortal cancer. Since there are no methods available – clinical, histopathologic, molecular, or other – that reliably distinguish mortal cancers from more innocent lesions, the risk for overdiagnosis and overtreatment becomes substantial notably when PSA-screening is used widely.

Given the lack of solid scientific evidence, this lecture will rather address conceptual issues in an attempt to summarize the advantages and the disadvantages of watchful waiting as well as radical local treatment.

1563

Can surgery provide cure in clinical T3?

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Radical prostatectomy is considered as a standard treatment for locally confined prostate cancer while for locally advanced (cT3) prostate cancer, surgery is traditionally discouraged. These patients have an increased risk of lymph node metastases and local or distant relapse. A combination treatment (radiotherapy with hormonal treatment) is now becoming popular in this particular patient category.

While several reports exist on the outcome of pathologically T3 tumors only few studies have been published on the value of surgery for clinically T3 tumors. Most of the reports have treated patients with combinations of surgery and hormonal treatment. From the available reports (Rotterdam, Würzburg and the Mayo Clinic) it is obvious that there is a high incidence of lymph node involvement. On the other hand these reports have also Shown that surgery can be performed with acceptable morbidity. From our own data, it became obvious that there is a relevant subgroup of clinical T3a patients that are amenable for a curative treatment option by radical prostatectomy. Patients with clinically obvious massive extracapsular extension (cT3b) or seminal vesicle invasion (cT3c) are not good candidates but patients with limited extracapsular extension and a low PSA proved to have a good five year PSA relapse free survival.

These data will need further confirmation in a multi-institutional setting. There is a subgroup of patients with locally advanced disease that can be cured by radical prostatectomy alone. Patients with even more advanced local disease will rather be candidate for a combined radiotherapy-hormonal therapy combination.

1564

Conformal radiotherapy for prostate cancer

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Three-dimensional conformal radiation therapy (3D-CRT) is a technique of high precision radiotherapy that targets a prescribed dose to the tumor conforming to its spatial configuration, while decreasing the dose to surrounding normal tissues. The latter leads to decreased normal tissue complications, and permits tumor dose escalation to improve local tumor cure. This paradigm was confirmed in a study of 1050 patients with localized prostate cancer treated between October 1988 and March 1998. Prostate biopsies performed at $\geq$2.5 years after radiotherapy showed that patients receiving 81 Gy had 6% positive biopsies, compared with 29% after 75.6 Gy ($p = 0.04$) 43% after 70.2 Gy and 57% after 64.8 Gy. Radiation doses of $\geq$75.6 Gy also significantly improved the 5-year actuarial PSA relapse-free survival. The overall grade 3 rectal and bladder complications was 1.5%. However, the 5-year actuarial risk of grade 2 rectal bleeding for patients receiving 75.6–86.4 Gy was 17% compared to 6% for those treated with 64.8–70.2 Gy ($p < 0.001$). The application of intensity modulated radiotherapy (IMRT) significantly improved the tumor conformality, reduced the exposure of normal tissues, and decreased the rate of grade 2 rectal bleeding. These data indicate that conformal radiotherapy represents an advancement in the ability to deliver the high radiation doses required to improve the local cure of prostate cancer.

1565

Androgen regulated gene expression in prostate cancer

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Androgens are required for the development of prostate cancer and at least 80% of tumouts respond to androgen deprivation therapy. However, progression to an androgen-independent (AI) state usually occurs and the tumours become increasingly refractory to hormonal manipulation or other therapies.

The mechanisms underlying this transition are unclear but androgen receptor dysfunction, via mutation, amplification or structural changes in the AR protein accounts for some cases although the frequency is controversial. We have examined the CAG microsatellite repents in the transcription activation domain of the AR gene and find limited polymorphism in prostate cancers with a significant predominance of 19 repeats.

We compared the androgen-sensitive cell line LNCaP to a clonal variant, LNCaPr, which is androgen insensitive, to identify differences in the gene expression profile using suppression subtraction hybridisation. Three genes