

sensitivities reopened the discussion with a new strategy: induction CT followed, in good responders, by XRT or, in poor responders, by S. To date, 3 randomised trials have been published with such a design. The VA trial on larynx and the EORTC 24891, for hypopharynx had similar conclusions. In both trials there was no difference in survival between this experimental approach and the standard treatment (S + postop XRT) but 50% to 66% of survivors could retain their larynx. In the French trial (GETTEC) only T3 larynx SCC were eligible. The survival was poorer in the experimental arm. A meta-analysis (MACH-NC) of the 3 trials concluded in a non significant trend for a better survival in the surgical arm but 58% of larynx could be preserved in the experimental arm.

Conversely, subtotal surgery may avoid performing, in selective cases, a total laryngectomy. Finally, notable advances have improved XRT results: new fractionation, acceleration, both or concurrent administration of XRT and CT.

Clearly, there are different ways to preserve the larynx function which are still to be compared. As a result, this approach still remains in the field of clinical research.

1207

### Chemoradiotherapy as treatment of choice in oesophageal cancer

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In a prospective randomized controlled trial of neoadjuvant chemoradiotherapy versus surgery alone for patients with Carcinoma of the oesophagus we have observed that multimodal therapy can downstage tumour size, node stage, lymphovascular invasion and radial margin involvement. A complete response was obtained in 25% of adenocarcinomas and 32% of squamous carcinomas.<sup>1</sup>

Surgery may not have been necessary in some of these patients. One patient who did not proceed to surgery because of a severe myocardial infarct was tumour free for 4 yrs before developing a recurrence. Of 2 patients in whom surgery were omitted because of deteriorating performance status, 1 survived 2½ yrs before developing a recurrence and 1 was tumour free at last review at 2 yrs. One patient survived 30 mths despite having an incomplete response. Nine further patients survived for short periods or are still being followed up.

[1] Walsh T., Noonan N., Hollywood D., Kelly A., Keeling N., Hennessy T., *A comparison of multimodal therapy & surgery for esophageal adenocarcinoma*. N. Eng. J. Med. 1996, 335/462-7.

1208

### Chemo-radiotherapy reduces the need for a permanent colostomy

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A permanent stoma can rarely be avoided during radical surgery for *squamous carcinoma (SCC) of the anus or for adenocarcinomas (adenas) of lower third of the rectum*. Since primary radiotherapy (XRT) yields colostomy-free survival rates of 60-80% for SCC, it should be considered primary treatment, with surgery for failures. However, for *adenas* the cure rate is below 50% for tumours over 5 cms diameter. After XRT for *adenas*, planned *local excision* is safe but for tumours >5 cms radical surgery with *pouch procedures* are preferred. Concomitant cytotoxic chemotherapy (chemo) appears to enhance the XRT-sensitivity of both tumours. In SCC three large phase III clinical trials have been demonstrated an improvement in local control when XRT is combined with 5-fluoracil (5-FU) with no major increase in toxicity. Similar improvements appear in non-randomised studies in *adenas*, but randomised studies have shown increased postoperative complications following chemo-XRT. Since the optimal chemo-XRT schedule has yet to be decided, phase I/II studies should be conducted on patients with advanced inoperable/recurrent *adenas* using drugs with known activity like raltitrexed, oxaliplatin or irinotecan.

1209

### Multimodality approaches in breast cancer: What have we learned?

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There is now an increasing need for a multidisciplinary approach to the treatment of early breast cancer to obtain a high local control rate and

survival. With this multidisciplinary approach, there is a high probability of preserving the breast.

An increasing number of patients with DCIS are being discovered due to screening programs. The preliminary results of clinical trials in DCIS demonstrate that radiotherapy can reduce the local excision after microscopically complete excision of tumors up to 5 cm. On the other hand, a longer follow up is still necessary to define which subgroup will benefit most from radiotherapy.

For stage I and II invasive breast cancer, breast conserving therapy (BCT) has been shown to result in equivalent survival rates to mastectomy. With the introduction of the sentinel node biopsy, the treatment morbidity is reduced considerably for a large number of patients. Patients younger than 35 years old have a higher locoregional recurrence rate after breast conserving therapy. The increased use of adjuvant chemotherapy has reduced the amount of local recurrences; it is uncertain what the contribution is to the results of BCT in younger patients.

The difference in treatment outcome, which varies per institute, has led to an intensive quality assurance program. This has proved most effective as the results of a major EORTC trial (>5500 patients) showed much less variation in locoregional recurrence rate between participating institutes.

1210

### Limb salvage for soft tissue sarcoma: Multimodal procedures or improved surgery?

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It is common observation that amputations for soft tissue sarcoma (STS) progressively decreased in the recent decades. In the same span of time different multimodal treatment policies were experienced to improve local and systemic control with an impact on survival: perioperative radiation therapy, adjuvant chemotherapy, isolated limb perfusion, and combinations. These adjuvant procedures are usually conceived to be responsible for improving limb salvage surgery, but their role was never proved. In the last 20 years the survival rate of patients with STS had a minimal improvement, if compared with the number of amputations which significantly dropped from 40/50% to 10/20%. We reviewed 1319 patients with extremity STS operated in our Institute in the period 1965-1998. The amputation rate stratified by years was respectively: 1965-, 75 = 71% (37/52 pts), 1976-CE85 = 16% (46/287), 1986-CE95 = 8% (61/764), 1996-CE98 = 3% (6/216). By their own any single procedure helped local control and conservative operations but in details: RT is the main adjuvant tool for local control, but its rationale, even if more standardized in the recent period, did not change grossly by years. Moreover the indication to RT, as for adjuvant CT, is usually decided postoperatively and has no role on the surgical choice between conservative versus ablative operation. Preoperative CT was employed in 143 cases (111 with intra-arterial delivery of Adriamycin): shrinkage of the lesion was documented in about 40% of cases, but the split from amputation versus conservative operation was estimated around 4%. More recently hyperthermic isolated limb perfusion chemotherapy seems to improve these conservative possibilities: we perfused 70 cases, mainly in the last five years and their final role in local control is still under evaluation, however not responsible of the important improvement reported between the CE70ties and the CE80ties. Surgical reconstructive methodologies and vascular prosthesis were employed in less than 10% (128/1319) of our operations and changed the surgical indication in favour of limb sparing surgery in less than 3%. In conclusion all adjuvant or sophisticated procedures are effective on local control but do not give reason for the dramatic drop of amputations that is mainly due to improved anatomo-surgical knowledge and practice.

1211

### Combination therapy for osteosarcoma

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Osteosarcoma, the most common primary bone cancer, usually afflicts adolescents and young adults. The primary is often located in an extremity, and micrometastases to lung or bone are almost ubiquitously present. In order to be successful, treatment must eradicate both the primary and all metastases. Today, this goal can frequently be achieved by combining surgery with systemic chemotherapy. The main aim of chemotherapy in this setting is the eradication of micrometastases. Most successful protocols include two to four of the drugs methotrexate, doxorubicin, cisplatin, and ifosfamide.