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Lung Cancer Therapy in the Elderly

SHOULD ELDERLY patients with small cell lung cancer be treated differently than younger patients? Of the population in the western world, 10–15% is over the age of 70. The life expectancy of this population is on average 15 years for women and 8–10 years for men. A substantial and increasing percentage of the new malignancies will occur in this age group. Up till now patients over the age of 70 with lung cancer were frequently excluded from clinical trials for different reasons, such as the disease's supposed more indolent behaviour, the impaired bone marrow tolerance of the elderly, the presence of a compromised renal and liver function interfering with drug clearance, concomitant chronic disease, the diminished life expectancy and their attitude towards intensive treatment.

Age is not a recognised independent negative prognostic factor in patients with lung cancer. Extent of disease, initial performance status and weight loss are such dominant prognostic factors, that, in retrospective studies in particular, it is impossible to determine the effect of age. A less extensive presentation, with a possible impact on prognosis, is not uncommon in the described patient population [1]. With advancing age drug metabolism may be altered due to an increase in the volume of distribution, a decrease in hepatic drug metabolism and in renal clearance. Negative interactions of cytostatic drugs with medication taken because of concomitant chronic disease, has not proven a major problem but warrants careful consideration when dealing with this patient population. Clinicians are becoming more and more aware that the conception that older patients with lung cancer should not be treated may be wrong. Furthermore, patients have been treated and cured with chemotherapy [2]; this is recognised and also reflected in a joint EORTC/National Cancer Institute meeting recently held in Venice, Italy to discuss the need for studies in the elderly and to determine age criteria [3].

There are retrospective studies on the effect of treatment of elderly patients with small cell lung cancer, as by Clamon *et al.* [4] and by Findlay *et al.* (p. 1597–1601). Although the results may be interesting, these studies can not solve the question how to treat lung cancer in the elderly. These studies have many drawbacks. Not stated is why patients were selected to be treated and others not. Treatment was not uniform. Dose schedules were not always optimal. The considerations leading to full dose or gentle chemotherapy are not clear.

These studies only show that chemotherapy can be given to a selected group of elderly patients, but reveal no guidelines how to treat which patients. In phase II studies both with single drugs [5, 6] and with combination chemotherapy [7, 8] it has been demonstrated that treatment is feasible. They do not answer the question if aggressive, conventional or gentle treatment for elderly patients is effective.

Time has passed for drawing conclusions from retrospective studies on the treatment of patients over 70 years. There is an under-representation of patients aged 75 years and older among patients with lung cancer seen at comprehensive cancer centres

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[9]. Elderly patients are less often included in clinical trials [10]. It is a well-known fact that patients treated according to a protocol have a significant survival advantage over those treated according to the free choice of the clinician [11].

Proper staging of the patients is mandatory. Stratification and randomisation is obligatory for a balance in prognostic factors and to exclude selection bias. Good definitions of what is aggressive, what is conventional and what is gentle treatment are needed. Is single drug treatment as effective as multiple drug chemotherapy? Is oral treatment as effective as intravenous? Is treatment in elderly patients more schedule dependent than in younger patients? Is it possible to predict the haematological reserve of these patients? Should haematopoietic growth factors be given routinely or only on indication? How disturbing are the concomitant illnesses these patients have, for a adequate chemotherapy? Is the reponse similar to that seen in the younger population?

These questions can only be answered in proper designed phase III studies with a large enough number of patients to draw valid conclusions. Only multicentre studies seem appropriate for this. Treatment of elderly patients should be part of the mainstream of oncological practice [12].

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Radiosurgery for Brain Tumours

THERE ARE many examples in medicine where advances in treatment are led by technology and not by intellectually satisfying pursuits. Nevertheless, the emergence of new techniques does not guarantee progress and the indiscriminate use of new and fashionable treatment methods has to be checked by careful clinical evaluation. Stereotactic radiotherapy (SRT) (or radiosurgery when in the hands of neurosurgeons) has hit the headlines as a new hope for brain tumour patients. It is undoubtedly a technologically advanced method of radiation delivery, but is it the clinical breakthrough often claimed?

What is SRT?

The principle of SRT is simple. It is a high precision technique of localisation and delivery of external-beam radiotherapy at present applicable to the treatment of intracranial lesions. Patients are immobilised in a neurosurgical-type stereotactic frame which acts as a point of reference for three-dimensional localisation on multimodality imaging. This allows for the precise localisation of a region of interest.

Irradiation is highly focused by arranging sources of radiation in a spherical distribution around the patient's head converging onto a small central point. This started life as "radiosurgery" delivered by a dedicated multiheaded cobalt unit with focused sources arranged in a hemisphere around a patient (so-called gamma unit or knife) [1]. Similar high-precision delivery can be achieved with a modern linear accelerator by multiple beams either as multiple arcs of rotation [2–6] or multiple fixed non-coplanar beams [7]. An alternative means of localised irradiation utilises the property of Bragg peak of heavy particles as cyclotron generated protons [8] or heavy charged particles [9]. All of these techniques represent stereotactically guided, conformal external-beam radiotherapy.

How does it help in practice? The high precision of tumour localisation makes it possible to irradiate a smaller volume of normal tissue with less margin for inaccuracy and highly focused treatment delivery reduces the amount of radiation to normal brain [7]. This may allow for a higher dose of radiation to the target while reducing or maintaining the dose to the surrounding normal tissue. Providing that the limitation of conventional technique is the radiation tolerance of normal brain surrounding the tumour, it may be possible with the use of SRT to give a higher dose to the tumour without increasing damage to normal brain. In any case this is the theory. In practice single-fraction SRT/radiosurgery has been successfully developed for the treatment of small inoperable intracranial arteriovenous malfor-

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