## Hyperthermia in Clinical Oncology

### H.S. Reinhold and J. Overgaard

THE CLINICAL application of hyperthermia has a strong biological rationale [1–3]. Experimental and clinical studies indicate that tumour control rates can be significantly enhanced if, for example, radiation therapy is combined with hyperthermia [4, 5]. If a tumour is heated one or more times to a temperature of  $43^{\circ}$ C or higher for an hour, the probability of response or permanent control increases substantially.

Nevertheless, some important problems remain. After about 15 years of experiments and technological developments in heat delivery and temperature measurement, it is clear that the application of a hyperthermic dose of sufficient intensity to a tumour is not simple. In the past the tumour temperature was measured with one thermocouple several times to give the "tumour temperature". Nowadays continuous multipoint thermometry is available, which indicates that it is not justified to speak about the tumour temperature but rather about a distribution of temperatures, which is heterogeneous not only in tumour space but also in treatment time. At the fifth European BSD-Users conference, in Noordwijk aan Zee and Rotterdam, The Netherlands (18-19 May 1990), which focused mainly on the clinical application of loco-regional hyperthermia as an adjuvant to radiotherapy or chemotherapy, T-90 (the temperature reached in time and space by 90% of the sampled points) emerged as one of the better indices of the efficiency of hyperthermia and therefore the therapeutic outcome [6, 7]. The hyperthermic level achieved depends not only on the amount of energy deposited in the tumour tissue but also on the cooling effect of blood flow [8, 9]. Many heating methods have been tried: electromagnetic devices (refs. 10-12 and L. Baert et al.), ultrasound [13], systems based on interstitial brachytherapy [14, 15] and perfusions with heated solutions [16, 17]. Important advances reported at the meeting included online evaluation of temperature distribution of modern hyperthermia equipment in conjunction with the development of mathematical models (refs. 18 and 19 and A.P.M. Zwamborn and P.M. van den Berg) to optimize heat application during treatment [20, 21]. For the immediate future it seems realistic to add non-invasive thermometry to the hyperthermia equipment as an important aid in localizing power distribution in the patient.

Apart from these technological developments, a serious concern was whether currently used experimental tumour systems are of any value for clinical research in hyperthermia (ref. 8 and S.B. Field *et al.*). This is a key issue because progress in clinical hyperthermia, with its strong dependence on factors such as sequence and interval with radiation [2] and chemotherapy [22], is derived from animal models [2]. Thus the question of the number of hyperthermia treatments required for optimum effect, as well as the sequence and interval between the modalities, is much discussed [23]. No consensus was reached at the meeting, other than that the treatment should be at a sufficiently high temperature (preferably  $43^{\circ}$ C) and last for about an hour.

An encouraging observation is that all the retrospective analyses of superficial hyperthermia (e.g. carcinoma of the breast and recurrences of this tumour [4, 24] and head and neck nodes) indicate that with increasing hyperthermia treatment level, significantly higher response rates are obtained [6, 7, 25]. In addition, some prolonged complete responses in pelvic chondrosarcoma were reported by the paediatric oncology service in Paris. The current indications for successful adjuvant deep hyperthermia are found mainly in sarcomas [6, 24-26] and abdominal carcinomas, especially those of the cervix, colon and rectum [24]. There is also a need to improve the present results in bladder carcinoma [27]. In addition, an increasing number of encouraging results with thermochemotherapy, applied regionally or with perfusion, are being reported [17]. The meeting emphasized that hyperthermia is finding a definite place in the treatment of cancer.

As regards assessing the impact of hyperthermia on health care, a prospective cost-benefit analysis is being done by the Department of Economics at Erasmus University, Rotterdam, based on the results from the Rotterdam phase III trial on loco-regional hyperthermia plus radiotherapy. Such analysis is important: determining the value of a new, cost-increasing treatment modality [28]. Preliminary findings suggest that for pelvic tumours the costs may be moderate (about 1800 ECU per life year saved).

The meeting emphasized that deep heating for the treatment of pelvic malignancies has become feasible, and that the results are encouraging. The Rotterdam phase III trial with the BSD-2000 machine has been started to identify whether addition of this treatment will be of real benefit.

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# News

#### **Tumour Response Monitoring**

A symposium on Tumour Response Monitoring and Treatment Planning will be held in Munich on 11–13 April 1991 to discuss recent advances and current developments in the field. The chairman of the symposium is Professor A. Breit and the meeting has been organised in close collaboration with the World Health Organization. Further information can be obtained from: ART 91 Scientific Secretariat, Institute für Radiologische Onkologie der TU, Ismaninger Strasse 15, D-8000 München 80, Federal Republic of Germany. Tel (49) 89 41 40 43 05, fax (49) 89 41 40 43 96.

#### **EORTC Addresses**

A reminder of the new EORTC addresses. The EORTC Executive Office is at 83 Avenue Mounier—Bte 10, B-1200 Brussels, Belgium—tel (32) 2774 16 40, fax (32) 2 772 36 75. The EORTC Data Center is at 83 Avenue Mounier—Bte 11, B-1200 Brussels, Belgium—tel (32) 2 774 16 11 (randomisation only [32] 2 774 16 16) fax (32) 2 774 35 45.

#### Société Français de Radiothérapie Oncologique

The Société Français de Radiothérapie Oncologique will hold its first national congress in Paris on 22–23 November 1990. Further details can be obtained from the secretariat: SOCFI, 14 rue Mandar, 75002 Paris, France. Tel (33) 1 42 33 89 94, fax (33) 1 40 26 04 44.

#### European Osteosarcoma Intergroup

The 16th meeting of the European Osteosarcoma Intergroup was held on 17 April 1990 at the Netherlands Cancer Institute. Dr J. van der Eijken was announced as the new chairman of the group.

The Cambridge Data Centre reported on the progress of several protocols: 80861 has 239 patients with an average entry rate of 62 patients per year. So far 155 patients have stopped or completed therapy. A clear shift towards conservative surgery is indicated. 80862 has a total of 83 patients and further details