Radiotherapy

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ESTRO/VARIAN Award Lecture

No abstract

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Comparison of two conditioning regimens in allogeneic bone marrow transplantation (ABMT): Emphasis on the role of total body irradiation (TBI) for "high risk" patients

Ph. Giraud[1,3], S. Danhier[3], C. Payen[2], A. Pons[1], N. Daly-Schveitzer[1], J.M. Cosset[3], M. Attal[2]. [1]*Dépt de Radiothérapie, Centre Claudius Regaud, Toulouse;* [2]*Service d'Hématologie, Hopital Purpan, Toulouse;* [3]*Dépt de Radiothérapie, Institut Curie, Paris*

Purpose: This retrospective analysis aimed at comparing the patients' outcome after two different preparative regimens (with or without TBI) for ABMT.

Methods and Materials: From January 1984 to December 1994, 171 patients with acute leukemia (AL, n = 97), chronic myelogenous leukemia (CML, n = 49), lymphoma (14) and aplastic anemia (11) were registered. Preparative regimen included cyclophosphamide with TBI (CTBI group, n = 117) or busulfan (CB group, n = 54). Median follow-up was 36 months (0.4–120). Two groups were constitued: a "standard risk" group (116) including patients with AL in first remission and CML in chronic phase, and a "high risk" group (55) presenting AL in relapse or refractory state, or with CML in accelerated or blastic phase.

Results: At 3 years, the outcome was similar for survival (58% vs 62%) and transplant-related mortality (74% vs 65%) between CTBI and CB groups. Relapses were less frequent in the CTBI group (10% vs 24%). "High risk" patients had a poorer survival and a higher relapse rate, especially in CB group (33% vs 64%). In multivariate analysis, decreased survival was associated with HLA incompatible transplants, interstitial pneumonitis, age, thrombopenia and "high risk" patients. Higher relapse rate was associated with CB group and no graft-vs-host disease.

Conclusion: CTBI provided an equivalent or better outcome than CB, particularly in "high risk" patients. CB could be an acceptable alternative for patients in whom TBI would not be feasible.

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Is acute mucositis dose limiting for altered fractionated radiotherapy?

B. Maciejewski, K. Skladowski. *Dept. of Radiotherapy, Cancer Center MSC Memorial Institute, Gliwice, Poland*

Purpose: To analyze the incidence and kinetics of acute mucosal reaction in radiotherapy for head and neck cancers depending on fractionation, dose intensity and overall treatment time.

Material and Methods: A review of 25 published data sets concerning conventional accelerated and hyperfractionated radiotherapy for head and neck cancer. Incidence, the onset and duration of healing of severe acute mucositis were analyzed in relation to accumulated dose per week, and Dose-Time Ratio (DTR) which is normalization factor expressing an average dose per day multiplied by an average fractions per day. Logistic regression analysis was used to estimate correlation between fractionation parameters and acute mucositis.

Results: It was found that incidence and the onset of acute mucositis strongly depends on accumulated dose per week (AD) and the risk of severe acute mucositis increases above 80% when the AD is larger than 14 Gy, and acute effect occurs sooner than on the end of second week of treatment. The risk of 100% of severe acute mucositis strongly correlates with accelerated fractionation. The risk significantly decreases to 40–20% when hyperfractionation is used.

Conclusions: For altered fractionation acute mucosal reactions became dose limiting. Acceptable risk of acute mucositis can be expected when accumulated dose per week is lower than 72 Gy and the DTR is below 2.5 Gy/day^2. High value of the AD (>14 Gy) and DTR above 10 Gy/day^2 lead to high risk of persistent confluent mucositis and consequential late necrosis.

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Is there a safe dose for spinal cord after hyperfractionated and conventional radiotherapy?

M. Niewald[1], W. Feiden[1], M. Kiessling[2], W. Berberich[3], U. Abel[2], W. Lehmann[1], N. Licht[1], W. Staut[1], C. Nieder[1], K. Schnabel[1]. [1]*Univ. Hosp. of Saarland, Homburg/Saar;* [2]*Univ. of Heidelberg,* [3]*St. Mary's Hospital Amberg, Germany*

Purpose: Animal experiments show that hyperfractionation spares spinal cord, but doses are not transferable from rodents to humans. We therefore tried to find out a "safe dose" for spinal cord using own clinical and literature data.

Patients and Methods: From standard radiotherapy techniques for ENT tumors (lateral opposing irregular portals, total dose 60–70 Gy (single dose 2 Gy) or 82.8 Gy (single dose 1.2 Gy twice daily) biologically effective dose (BED, a/β = 2.0 Gy) to the spinal cord was recalculated. In total, 1008 patients had been irradiated in that way. In 802 of them, planning target volume had to be extended to the posterior cervical lymph nodes, thus to the spinal cord. Aditionally, we tried to recalculate BED from 60 data sets taken from literature.

Results: In our patients, BED to spinal cord varied from 7.7 to 83.8 Gy_2. **We never saw signs of myelopathy.** Additionally, from 48 out of 60 papers BED could be calculated. Here myelopathy did not or very rarely occur after a BED of not more than 90 Gy_2.

Conclusion: Our data and those taken from literature indicate that a BED to spinal cord of 90 Gy seems safe. This relies to a conventional dose of 45 Gy (single dose 2 Gy) or a hyperfractionated dose of 56.5 Gy (single dose 1.2 Gy twice a day).

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N-oxide derivatives of chlorambucil as agents for overcoming hypoxic cell radiation resistance

M.R. Horsman[1], D.W. Siemann[2], D.J. Chaplin[3], D.L. Kirkpatrick[4]. [1]*1 Danish Cancer Society, Department of Experimental Clinical Oncology, Aarhus University Hospital, Denmark;* [2]*Department of Radiation Oncology, University of Florida, Gainesville, USA;* [3]*Gray Laboratory Cancer Research Trust, Mount Vernon Hospital, Northwood, UK;* [4]*Department of Chemistry, University of Regina, Regina, Canada*

Purpose: To develop and test N-oxide (N-O) derivatives of chlorambucil (CL). The rationale being that the N-O group should deactivate CL thereby reducing systemic toxicity, but under hypoxic conditions, seen in most solid tumours, this N-O group will be reduced thus reactivating the drug.

Methods: Drugs were i.p. injected into CDF1 mice, with a 200 mm^3 C3H mammary carcinoma grown in the foot, before/after local tumour irradiation (15 Gy). The endpoint was tumour growth time (TGT; time to grow to 600 mm^3).

Results: CLN-O showed >2-fold less systemic toxicity than CL itself. At the highest dose tested (100 mg/kg) CLN-O increased the mean (± 1 SE) TGT for control mice from 4.8 (± 0.2) to 6.5 (± 0.4). It also increased the TGT for radiation from 16.4 (± 0.7) to 19.1 (± 1.1); this effect being independent of sequence and interval. Similar results were seen with an ethyl CLN-O derivative, although the benzyl form was more toxic. Comparable findings were seen in KHT tumours using an excision assay.

Conclusions: Some N-O forms of CL can decrease drug-induced systemic toxicity, while showing potent activity against hypoxic tumours.

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An obvious and underestimated predictive assay: Precise, cheap and easy prediction of radiotherapy outcome using tumor volume

Hans-Hermann Dubben[1], Hans-Peter Beck-Bornholdt[2]. [1]*Department of Radiotherapy;* [2]*Institute of Biophysics and Radiobiology University of Hamburg, Martinistrasse 52, 20246 Hamburg, Germany*

Purpose: A research strategy in radiotherapy is to develope assays that allow prediction of tumor response which in turn enable individualized prognosis and treatment decisions. For this purpose a wide variety of assays is currently being explored. In this contribution, the impact of tumor volume on radiotherapy outcome and its predictive potential is investigated.

Method: Re-evaluation of clinical data from the literature.

Results: Tumor volume significantly influences radiotherapy outcome. Tumor stage reflects tumor size only partially; it is mainly correlated to surgical operability. Tumors even of identical stage vary by factors of more