QUALITY OF LIFE IN PATIENTS WITH LOCALLY ADVANCED PROSTATE CANCER TREATED BY RADIOTHERAPY PLUS HYPERTERMIA.

Maluta S *, Marciai N, Pioli F, Nadalini L°, Corsi A°, Benechini PL.°, Gacci M.†, Apolone G‡, Dall’Oglio S*, Giri MG°°°

Radiotherapy Dpt., °°°Medical Physics Dpt., °Psyco-oncology Unit of University-Hospital of Verone, °° Urology Dpt of Parma, †Urology Dpt of University of Florence, ‡Mario Negri Institute, Italy

Introduction. In locally advanced prostate cancer (LAPC) Conformal Radiotherapy (CRT) should be considered the first therapeutic option. CRT and IMRT, allowing a dose more than 80 Gy, may increase local control providing that patients accept a higher risk of rectal complications. Although dose-response data suggests that higher dosage is generally better, it is difficult to determine how much of the improvement in biochemical control is simply related to better patient selection or the better delivery of irradiation. Rectal grade 2-3 complications increase from 12 to 26% when dose is raised from 70 to 78 Gy. The use of Local Hyperthermia (LHT) combined with radiotherapy at intermediate dose should avoid the dose escalation hazards. LHT does not increase late effects when added to radiotherapy and it seems to enhance efficacy of combined treatment (Anscher 1997, Kalapurakal 2000). It is feasible and well tolerated allowing a heat uniform distribution in the prostate and in seminal vesicles, with optimal temperature levels. The primary endpoint of this study was to evaluate quality of life of patients treated by using radiotherapy and local hyperthermia. Secondary endpoints: to evaluate freedom from biochemical recurrence, disease-free survival, and overall survival.

Materials and method. From January 2000 to December 2004, 107 patients with LAPC were treated by using CRT plus LHT. Mean PSA levels and Gleason score of these patients were 13 ng/ml (range 6-90) and 7 (range 6-9), respectively. All patients were treated by using conformal radiotherapy (CRT) at median dose of 74 Gy (range 68-78 Gy) with fractionation of 2 Gy/fraction/5 fractions per week, delivered with six-field isocentric conformal radiotherapy by using MLC and photons of 6 or 10 MV. The clinical target volume (CTV) included prostate and seminal vesicles with a margin of 5 mm. LHT was delivered after radiotherapy session, 1 session/week during the four week of the radiotherapy course (mean maximum temperature of 41.17°C, and mean T90 of 40.36°C), by using BSD 2000 with Sigma-60 applicator®. Androgen suppression therapy (AST) was performed in 73 patients 3-6 months before the start and during the course of CRT as neoadjuvant-concomitant therapy, whereas in 57 patients AST was administered as adjuvant therapy. Of these patients 74 were recently recruited in a prospective study evaluating quality of life (QoL) by using UCLA Prostate Cancer Index (UCLA PCI) and Medical Outcome Study 36-item SF (SF 36) questionnaires modified for Italian people. Mean age of this group was 73.1 (-31.3 / +12.7). To evaluate the sexual function it’s important to note that the majority of these patients were married (81%), 12.2% were single, and 6.8% widowed.

Results. Among 107 patients, 13 (12.1%) died for progression disease, whereas 3 patients (2.8%) died for intercurrent disease. The UCLA PCI was delivered to all patients enrolled in the study, whereas SF 36 questionnaire was administered only to 54% of patients examined. In terms of late toxicity, only 2 patients (1.8%) reported grade 2 GI injuries. No late GU severe complications were reported. Only 5 patients (4.6%) experienced a grade1 toxicity. Twenty-one patients (28.3%) achieved a normal sexual activity after AST interruption, considering the mean age of these patients.

Conclusions. In the randomized phase III study of MDACC 26% of patients treated with 78 Gy experienced a grade 2 rectal toxicity, whereas Zelefsky, by using IMRT reported only 4% of grade 2 GI. Unfortunately, he found a higher (15%) GU toxicity. In our patients grade 2 GI rate is very low and very few grade 1 GU late complications were reported. In LAPC, LHT plus CRT at intermediate dose is a promising approach useful to enhance irradiation effectiveness without increasing treatment toxicity.