Further associations were sought with patient prognosis, and the important histopathological features of Breslow's thickness, Clarke's levels of invasion, mitotic rate, inflammatory cell infiltrates and tumor ulceration.

**Results:** HIF1a and HIF2a expression by melanoma cells was correlated directly with VEGF expression. HIF1a expression was more frequent in cases with low mitotic index, but there was no association of HIFas with other histopathological variables. Tumors having high VEGF or HIF2a expression were associated with a poorer prognosis in both univariate and multivariate analysis. The value of Breslow's thickness and Clarke's levels in prognosis was reaffirmed, although only in univariate analysis.

**Conclusions:** Overexpression of HIF1a and HIF2a are linked to VEGF expression in nodular malignant melanomas. HIF2a and VEGF are important prognostic factors in melanoma.

# Genitourinary cancer

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## Quality assurance in conformal prostate radiation therapy: technology questionnaire for EORTC trial 22991

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For the EORTC Radiotherapy Group Purpose: A technology questionnaire is designed to evaluate the abilities of participating centres to comply with the required procedures in EORTC trial 22991 for high dose three-dimensional conformal radiotherapy (3D-CRT).

**Materials/Methods:** Questionnaires on imaging (CT) data acquisition, treatment planning, delivery and verification systems and data transfer systems were sent to the participating centres (n=31). Over 50 questions covered the technical infrastructure used for the compulsory and optional procedures described in the protocol. The frequency of basic verification and calibration of geometrical and mechanical parameters was documented as well.

**Results:** All centres replied to the questionnaire. The vast majority (>95%) of questions was completed. All centres have appropriate CT slice thickness and matrix size to acquire images with good resolution and to allow satisfactory 3D reconstruction. All centres use beams eye views to shape treatment fields and all but 2 produce digitally reconstructed radiographs (DRR) to display treatment fields. All centres can generate dose-volume histograms of the organs of interest. 3D dose calculation algorithms are available in all centres except one. The data including DRR, isodose charts and treatment reports can be transported by hard copy or image format in more than half of the centres and rarely by DICOM or by manufacturer specific format. Treatment verification is done by only conventional portal imaging (6), EPID (11) and both (14). In vivo dosimetry, optional in this trial, is done with only diodes (6), only TLD (1) or more than one option (7). There is a variation in the frequency of the QA procedure of external beam units, however the results are in accordance with the international accepted tolerance levels and practice guidelines.

**Conclusion:** The results of questionnaire confirm that participating centres have access to the relevant equipment and can cope with the procedures which are necessary to deliver 3D-CRT properly according to the trial recommendations.

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## Prognostic factors in advanced nonseminomatous germ cell tumors (NSGCT): importance of primary tumor (PT) histology and numbers of negative prognostic factors (NPF).

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**Purpose:** Generally accepted IGCCCG classification has some limitations the main of which is the absence of data about histology subtypes. In our study we retrospectively studied prognostic relevance histology as well as other factors in advanced NSGCT.

**Patients and methods:** 482 NSGCT CT-naïve pts treated with modern etoposide-based CT in our department during 1987 2001 were included in the analysis. Median f.-up time was 39 months. The end-point of the study was overall survival (OS). Cox regression analysis was used on these data. All markers levels were defined as *log* of absolute values.

**Results:** Multivariate analysis revealed the following prognostic factors as independent: presents of teratoma in PT (hazard ratio (HR) 1.59; 95% confidence interval (CI), 1.04-2.44), ±-fetoprotein (AFP) level (HR 1.14; 95% CI, 1.06-1.23), lactate dehydrogenase (LDH) level (HR 1.56; 95% CI, 1.20-2.01), presence of nonpulmonary visceral metastases (NPVM) (HR 2.23; 95% CI, 1.32-3.77), and mediastinal PT (HR 3.17; 95% CI, 1.44-7.00). 3 prognostic groups were distinguished: good prognosis (testis/retroperitoneal PT, absence of teratoma in PT, AFP level < 1000ng/ml and LDH level < 1,5 x upper limit of normal (ULN) range); intermediate prognosis (testis/retroperitoneal PT, presence of teratoma in PT, either AFP level ≤10000ng/ml, LDH level 1,5-10xULN or AFP level 1000-10000ng/ml, LDH level ≤ 10xULN); poor prognosis (either mediastinal PT, presence of NPVM, AFP level >10000ng/ml or LDH level >10xULN). Depending on the number of NPF intermediate and poor prognostic groups can be divided into two (see table).

| Proposed prognostic groups | No. of pts | 3-years OS (95% CI) | 1 NPF 3-years OS (95% CI) | 2 NPF 3-years OS (95% CI) | 3 NPF 3-years OS (95% CI) |
|---|---|---|---|---|---|
| Good | 21% | 92% (87 - 98) | – | – | – |
| Intermediate | 59% | 76% (73-82) | 83% (75-89) | 69% (45-83) | 50% (29-71) |
| Poor | 20% | 45% (34-55) | 49% (37-61) | 28% (7-49) | – |

**Conclusions:** The analysis showed negative prognostic significance of teratoma elements in PT and numbers of NPF for advanced NSGCT pts. It should be taken into account for planning of treatment of these pts.

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## The effect of total radiation dose and overall treatment time on local control for bladder cancer

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**Purpose:** To evaluate the influence of total radiation dose and overall tratment time on local control in patients with T2, T3 bladder cancer treated with radical radiotherapy.

**Material and Methods:** The analysis is based on 480 patients with T2, T3 bladder cancer, who were irradiated at the Center of Oncology in Gliwice between 1975 and 1995. There were 35% of patients with T2 and 65% of patients with clinical stage T3 bladder cancer. Radiotherapy was performed with photons X 9-23 MV or $Co^{60}$. Total radiation dose (TD) ranged from 59,2 Gy to 72 Gy (mean- 65.5 Gy), overall treatment time (OTT) ranged from 30 to 91 days (mean- 51 days). The fractionation schedules were as follows: **1.** conventional fractionation (once a-day, dose per fraction of 1.8-2.0 Gy, mean TD- 65.4 Gy, mean OTT- 53 days), **2.** protracted fractionation (once a-day, dose per fraction of 1.6-1.7 Gy to pelvis and dose per fraction of 2.0 Gy to boost, mean TD- 65.4 Gy, mean OTT- 62 days), **3.** accelerated boost (pelvis irradiated once a-day with dose per fraction of 2.0 Gy, boost twice a-day with dose per fraction of 1.3-1.4 Gy, mean TD- 66 Gy, mean OTT- 45 days), **4.** accelerated hyperfractionation (both pelvis and boost irradiated twice a-day, dose per fraction of 1.2-1.5 Gy, mean TD- 65.6 Gy, mean OTT- 41 days). In 261 patients (54%) there were planned and unplanned gaps during radiotherapy. Local control probability was estimated using the logistic regression with application of LQ-model. In the second step of the analysis the Cox regression was used.

**Results:** With the median follow-up of 76 months, the actuarial 5-year local control rate was 47%. In both the logistic regression and the Cox regression, total radiation dose (p=0,01 and p=0,009, respectively) and overall treatment time (p=0,03 and p=0,04, respectively) were independently correlated with local control. Using the logistic regression the estimated time factor was 0.21 Gy/day, which means that prolongation of overall treatment time for one day requires the extra dose of 0.21 Gy for the same probability of local control.

**Conclusions:** This study demonstrates that total radiation dose and overall treatment time might be the important factors for local control in bladder cancer.