Materials/Methods: Since December 1991 until August 2002, 49 patients with completely resected gallbladder cancer have been treated adjuvantly with radio-chemotherapy. Surgical treatment was cholecystectomy and lymph node resection. 19/49 patients underwent re-operation. Radiotherapy consisted of either Whole Abdomen Irradiation with a boost to the tumor bed in 19 patients or tumor bed only in 30 patients. Chemotherapy was given concomitantly with radiotherapy, and consisted of 5-fluoruracil in 41 patients and Gemcitabine in 9 patients. No further chemotherapy was given.

Results: Twenty four patients have failed, and 17/24, (71%) have done so by two years. With a minimum follow up of 24 months, 31 months median, 44 months mean, the overall survival rate is 52% at 5 years. Treatment was tolerated fairly well, with only 3 patients (6%) unable to finalize their treatment and 5 (10%) with interruption of the treatment. The other patients were able to complete their treatment with no interruptions.

Conclusions: Adjuvant radiochemotherapy is a safe and useful treatment for gallbladder cancer after a macroscopically complete resection. The results achieved of 52% survival at 5 years in patients who have had a complete macroscopic resection, compares favorably with the survival reported after surgery alone for those patients.

2095 Helical Tomotherapy SBRT for Liver Metastases: Recommendations for Potential Candidates Based on Tumor Size and Location

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Purpose/Objective: Stereotactic Body Radiotherapy (SBRT) has been shown to be effective for local control of metastatic liver tumors. Several groups have shown that liver SBRT is well tolerated with schedules ranging from 20–40 Gy in 2–4 fractions or 14-26 Gy in 1 fraction. Reported side effects include transient fever, nausea, and vomiting, and mildly symptomatic grade 1 and 2 radiation-induced liver dysfunction. Currently Phase II trials are examining SBRT of liver with doses of 60 Gy in 3 fractions. HiArt Helical TomoTherapy is a treatment unit which delivers co-planar helical IMRT that is capable of image guided SBRT. In order to determine if Helical Tomotherapy could be used for SBRT of liver tumors we performed inverse treatment planning and analyzed the dosimetry for multiple liver GTV volumes in several representative anatomic locations. The purpose of this study was to develop objective criteria for defining the suitability of liver tumors for Helical Tomotherapy SBRT based on tumor size and proximity to normal organs.

Materials/Methods: Hypothetical liver lesions were created using an existing CT scan. These GTV lesions were of sizes from 1 to 6 cm in diameter with GTV volumes ranging from 0.8 cm^3 to 84.8 cm^3. The liver was subdivided into the left lobe, right upper lobe, and right lower lobe and the GTV structures were placed in each of these liver subdivisions. A 5mm radial expansion and a 10mm craniocaudal expansion of the GTV was used to create the PTV. Treatment plans were generated using the Helical Tomotherapy inverse planning system with a minimum PTV dose of 60 Gy in 3 fractions covering at least 95% of the PTV. We chose to use the 25 mm jaw width after preliminary calculations revealed that the 10 mm jaw width would require over 2 hours to deliver a 20 Gy dose even for small tumors. Normal organ constraints were as follows: 30 Gy maximum dose to the heart, stomach, and small intestine; 18 Gy maximum dose to the spinal cord; 700 cc of normal liver to receive < 15 Gy; 35% of the kidneys to receive < 15 Gy. For a plan to be considered acceptable all of the target and normal organ constraints had to be met.

Results: Analysis of the dosimetry revealed differences in limitations to treatment by liver subdivision. For the left lobe, proximity to the heart and stomach limited the size of lesion with acceptable dosimetry to 3 cm. For the right upper lobe, the proximity to the heart and liver dose volume constraints resulted in a maximum treatable tumor size of 5 cm. A tumor size of 5 cm was limiting for the right lower lobe, again due to normal liver dose volume constraints; however proximity to the small bowel was also a limiting constraint. Dose inhomogeneity was acceptable, with the maximum doses ranging from 62 Gy - 77 Gy. Calculated treatment times varied between 58–85 minutes.

Conclusions: The HiArt Helical Tomotherapy system is capable of performing high dose liver SBRT that meets the specified target and normal organ constraints. This study provides broad initial screening eligibility criteria for patients with hepatic metastases who may be suitable for TomoTherapy-based liver SBRT. These guidelines are: for left lobe tumors; a GTV of $\leq$ 3 cm in diameter and a GTV that is at least 13 mm from the heart and 8 mm from the stomach; for right upper lobe tumors; a GTV of $\leq$ 5 cm in diameter that is at least 13 mm from the heart; for right lower lobe tumors; a GTV of $\leq$ 5 cm in diameter that is at least 8 mm from small bowel.

2096 Bicalutamide 150 mg in Addition to Standard Care Delays Progression to Bone Metastases in Patients with Locally Advanced Prostate Cancer: Analyses From the Second Analysis of the Early Prostate Cancer Program

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Purpose/Objective: The non-steroidal antiandrogen bicalutamide ("Casodex") offers potential quality-of-life advantages over castration-based therapy in the management of physically and sexually active patients with prostate cancer. The ongoing bicalutamide Early Prostate Cancer (EPC) program is the first study to evaluate a non-steroidal antiandrogen adjuvant to radiotherapy of curative intent. This program comprises 3 double-blind, randomized, placebo-controlled trials in which patients with localized or locally advanced disease received bicalutamide 150 mg/day or placebo in addition to standard care (radical prostatectomy [RP], radiotherapy [RT], or watchful waiting [WW]). Combined results from the second protocolled analysis (median follow-up 5.4 years) showed that in patients with locally advanced prostate cancer bicalutamide significantly improved progression-free survival (PFS) versus standard care alone (Wirth et al 2004). Bone metastases, which develop in $>$80% of patients with advanced prostate cancer, are associated with significant morbidity and are one of the most costly complications of the disease. Here we report the results of an exploratory analysis from the EPC database on the effect of bicalutamide on metastatic PFS, focusing on patients with locally advanced disease.

Materials/Methods: Risk of bone metastases was assessed as the number of progression events, defined as either bone scan-confirmed progression or death from any cause in the absence of bone scan-confirmed progression. Data for patients with locally advanced disease randomized to bicalutamide or standard care alone were analyzed using a Cox proportional hazards regression model.

Results: Bicalutamide 150 mg/day significantly improved metastatic PFS, reducing the risk of bone metastases by 35% compared with standard care alone in patients with locally advanced disease (hazard ratio [HR] 0.65; 95% confidence intervals [CI] 0.56, 0.76; $p<0.0001$). There were 290 progression events (7.2%) in the bicalutamide group, 121 confirmed by bone scan and 169 deaths from any cause in the absence of bone metastases; 348 progression events (8.6%) occurred in the placebo group, 204 confirmed by bone scan and 144 deaths from any cause in the absence of bone metastases. In the locally advanced group, a reduced risk of bone metastases was also observed when data were analyzed by primary therapy.

Conclusions: Bicalutamide 150 mg/day in addition to standard care significantly improves metastatic PFS, reducing the risk of bone metastases in patients with locally advanced prostate cancer irrespective of primary therapy. Therapy with bicalutamide 150 mg should, therefore, extend the time free from medical complications, leading to an improvement in disease-related morbidity. The EPC program is ongoing, with patients continuing follow-up for progression and survival.

'Casodex' is a trademark of the AstraZeneca group of companies.

Analysis of metastatic progression events for patients with locally advanced disease

		No. events (% of patients)			
Primary therapy	No. patients	Bicalutamide 150 mg/day*	Standard care alone	HR (95% CI)	p-value
RP/RT	2024	153 (14.8)	177 (17.8)	0.73 (0.59, 0.91)	0.0054
WW	657	136 (40.6)	171 (53.1)	0.57 (0.45, 0.71)	

* 1 patient with a progression event received cryotherapy as standard care and therefore is not included in this table

2097 Predictors of Rectal Acute Toxicity in High-Dose 3D-CRT for Prostate Cancer. Results From a Prospective Multi-Centric Study Performed by the AIRO National Working Group on Prostate Irradiation

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Purpose/Objective: Clinical, dosimetric and technical parameters affecting acute rectal toxicity (TOX) were prospectively investigated (AIROPROS 01–02 trial) in prostate cancer patients (pts) treated with high dose conformal radiotherapy (CRT). Acute TOX were evaluated using RTOG/EORTC scoring system and a self reported questionnaire.

Materials/Methods: Prerequisites for the study were: 1. TOX scoring scales previously discussed and accepted; definition and validation of a self-assessed questionnaire on rectal TOX; 2. contouring consistency (previously accepted rectum length definition); 3. dummy run on rectum contouring; 4. dosimetric consistency in dose and DVH calculation. Between July 2002-December 2003, 1132 pts entered this national cooperative study. CRT doses were 70–80 Gy (ICRU dose: median 74 Gy) at 1.8/2 Gy/fr. A self reported 11 items questionnaire (focused on: frequency, tenesmus, continence, pain, bleeding and use of drugs) was administered before treatment and at its end and RTOG/EORTC TOX during and just after the end of the therapy recorded. The correlation between mean/max rectal dose, rectal volume, ICRU dose, pre-treatment morbidities, hormonal therapy (AD), drug prescription, presence of diabetes or hypertension, pelvic nodes irradiation and rectal TOX was investigated by uni- and multi-variate (MVA) logistic analyses. Concerning the questionnaire results, only moderate to severe TOX were analysed, excluding for each question patients showing a baseline high score in the first questionnaire (i.e.: before the treatment).

Results: Concerning RTOG/EORTC TOX, pts with grade 1, 2 and 3 TOX were 279, 290 and 6. Considering grade 2–3 acute TOX, AD resulted to be protective in univariate analysis; however, this was not confirmed in MVA where the mean rectal dose was the most predictive variable ($p=0.0004$, OR=1.03) together with pre-existing hemorrhoids ($p=0.057$, OR=1.33) and pelvic node irradiation ($p=0.06$, OR=1.67); the use of anticoagulants was found to be protective ($p=0.002$, OR=0.62). When considering together grade 1–3 acute TOX, mean dose was confirmed to be the most predictive variable ($p\leq0.0001$, OR=1.03) as well as pelvic nodes XRT ($p=0.06$, OR=1.68). The questionnaire-based scoring (moderate to severe symptoms) revealed: a) a higher mean rectal dose is associated with higher risk of bleeding ($p=0.009$, OR=1.04); b) larger irradiated volumes are associated with increased frequency, tenesmus, incontinence and bleeding ($p=0.007–0.07$; OR=1.4–8.9); c) AD is protective with regard to frequency ($p=0.002$, OR=0.32) and tenesmus ($p=0.025$, OR=0.52); d) pre-existing hemorrhoids are associated with a higher risk of tenesmus ($p=0.01$, OR=1.99) and bleeding ($p=0.03$, OR=1.73); e) hypo-glycemic drugs are highly associated with diarrhea ($p=0.001$, OR=5.84).