achieved within five years in 76.9% versus 86% for patients with a D90 > 140 Gy, (p=.03). For patients with a Gleason score of <6, a PSA of 0.2 was achieved in 5 years by 86% of patients versus 83% for those with scores of 6 (p=.01).

**Conclusions:** PSA decline following I-125 implantation is a slow process with a median time to nadir of 4.3 years and declining values seen up to 10 years. Larger volumes and higher dose implants result in a faster decline in PSA with greater percentages of patients reaching a nadir value of 0.2 by 5 years.

## 2098 Interfractional Variation in Position and Volume of the Uterus During Radical Radiotherapy for Cervical Cancer

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**Purpose/Objective:** Recently, intensity-modulated radiotherapy (IMRT) has been applied to gynecological malignacies. Several studies reported that 3-dimensional conformal (3DCRT) and IMRT in the treatment of gynecological malignancies was superior to conventional whole pelvis irradiation in dose conformity to PTV and in reducing the irradiated volume of normal tissues. This study was conducted to investigate the positional change of uterus during radiotherapy, which can degrade the accuracy of 3DCRT and IMRT.

**Materials/Methods:** From 1997 to 2001, 66 patients received radical radiotherapy for cervical cancer in Samsung Medical Center. For each patient, two MRI scans were taken; one before the beginning of radiotherapy treatment and the other 3-4 weeks after radiotherapy. In T2 weighted MRI images, the positional change of the uterine was quantified by measuring six quantities; the distance from the cervix os to the isthmus of the uterus (Dcx), the maximum length from the isthmus of the uterus to the uterine fundus (Dco), the maximum vertical distance of the uterine body (Dco-per), the angle between the vertical line and the cervical canal in sagittal images (Acx), the angle of the uterine corpus from the vertical line in sagittal plan (Aco), and the relative angle of the uterine corpus from a fixed anatomical landmark in axial images (Aco-axi).

**Results:** More than 10 mm of the mean value of Dcx was decreased in 27 patients (41%) and Dco decreased more than 10 mm in 15 patients (23%). The mean reduction of Dcx plus Dco was 14.1 mm and more than 30 mm was reduced in 7 patients (11%), all patients had more than 4 cm of tumor size. The change in Acx ranged from 0.1° to 67.8° (mean 12.5°) and a difference of more than 10° was observed in 30 patients (46%). Aco changed 84.8° in maximum (mean 15.4°) and changed more than 10° in 37 patients (56%). Among 44 patients of anteflexed uterus, 5 patients changed into retroflexed uterus during treatment. 12 patients (18%) had more than 30° variation in any of the angles. The difference between Dcx + Dco regarding age and tumor size had significant relations. In the age group below 60 years, the mean value of change of Dcx + Dco was larger than that in the age group above 60 years (17.7 mm vs 11.9 mm). The difference of Dcx, Dco and Dcx +Dco in tumor size groups reached a statistical significance. The mean value of change in Dcx + Dco during the treatment was 8.0 mm in small tumors (maximum diameter <4 cm) and 17.9 mm in large tumors (maximum diameter ≥4 cm). In the age group below 60 years, the mean difference in Acx was statistically significant (17.5° vs 9.5° ) compared with the age group above 60 years.

**Conclusions:** Positional changes of the uterus during radiotherapy should be considered in the treatment planning of 3DCRT or IMRT, particularly in patients under 60 years or those with tumor size greater than 4 cm.

## 2099 Prognostic Significance of Decreased E-Cadherin Protein Expression in Pathologic Stage I - III Endometrial Cancer: An Immunohistochemical Analysis

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**Purpose/Objective:** E-cadherin is a membrane glycoprotein that mediates cell-cell adhesion in normal endometrial tissue. Decreased E-cadherin expression is associated with deep myometrial invasion, high grade, and papillary and clear cell histologies in endometrial cancer. However, the relationship between E-cadherin expression and clinical outcome is not clear. The purpose of this study is to examine the relationship between decreased E-cadherin expression and outcome in pathologic stage I-III endometrial cancer.

**Materials/Methods:** The cohort consisted of 107 patients diagnosed between 1992 and 1998 with pathologic stage I (84 cases), II (15 cases), or III (8 cases) endometrial cancer. We omitted 4 cases with sarcoma or spindle cell cancer, 3 cases for whom tissue could not be obtained, 1 case receiving pre-operative radiation therapy, and 1 case for whom follow-up was unavailable. Immunohistochemical analysis of hysterectomy specimens from the remaining 98 cases was performed using a monoclonal antibody directed to E-cadherin. Specimens were divided into four categories based on percentage of tumor cells with normal membranous expression: A (>75%), B (25-75%), C (5-25%), and D (< 5%). For the purposes of analysis, category D was defined as low expression. Expression was evaluated by two observers (AGM, JJM), who were blinded to outcome. Outcomes including cause-specific survival (CSS), progression-free survival (PFS), and extra-pelvic failure were obtained from chart review and tumor registry data. Univariate analysis was performed using the method of Kaplan-Meier applying the log rank test. Prognostic models used multivariate Cox proportional hazards, adjusting for age, race, stage, myometrial invasion, grade, lymphovascular space invasion (LVSI), unfavorable histology (papillary serous or clear cell), chemotherapy, and radiation therapy. Multivariate logistic regression was used to evaluate the association between E-cadherin expression and stage, grade, unfavorable histology, and myometrial invasion.

**Results:** E-cadherin expression in each category was as follows: A (24%), B (26%), C (19%), D (31%). With a median follow-up of 59 months (range: 4-152), there were 30 deaths (10 of 30 from endometrial cancer). Overall 16 patients developed recurrent disease (6 pelvic, 9 extra-pelvic, 1 both). Five-year actuarial outcomes comparing patients with low expression to all other categories were as follows: CSS (78.9 vs. 94.6%, p=0.066), PFS (69.2 vs. 90.8%, p=0.024), and extra-pelvic failure (21.7 vs. 4.9%, p=0.055). Adjusted hazard ratios with 95% confidence intervals (CI) were as follows: cancer death (HR=6.11, CI

1.19-31.5, p=0.03), any failure (HR=4.39, CI 1.36-14.1, p=.01), and extra-pelvic failure (HR=5.67, CI 1.17-27.5, p=0.03). High grade, deep myometrial invasion, LVSI, advanced stage, and unfavorable histology were associated with elevated risk of all outcomes. Patients with low E-cadherin expression were more likely to have tumors with papillary serous or clear cell histology (OR=1.83, CI 0.54-6.15, p=0.33), and grade 3 (OR=1.77, CI 0.47-6.64, p=0.40) but these differences were not statistically significant.

**Conclusions:** Low E-cadherin expression in stage I-III endometrial cancer is associated with a statistically significant decrease in progression-free survival and increases in the risk of extra-pelvic progression and endometrial cancer death, independent of known prognostic factors. Evaluation of E-cadherin expression may have clinical importance in selection of patients for adjuvant therapy.

## 2100 A Randomized Clinical Trial on Continuous 7-Day-a-Week Postoperative Radiotherapy in High-Risk Squamous Cell Head-and-Neck Cancer: A Preliminary Report on Acute Normal Tissue Reactions

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**Purpose/Objective:** To evaluate acute normal tissue reactions in patients treated with continuous accelerated postoperative irradiation (p-CAIR) vs. conventionally fractionated postoperative radiotherapy (p-CF).

**Materials/Methods:** Between October 2001 and December 2002 100 patients with squamous cell cancer of the larynx, oral cavity, oropharynx or hypopharynx, after major surgical intervention, with high-risk pathologic features, and no gross residual disease were recruited for this trial. The patients were randomly assigned to receive 63 Gy in 1.8 Gy 7-day-a-week fractions over a period of 5 weeks (n=48), or 63 Gy in 1.8 Gy fractions given Monday to Friday over 7 weeks (n=52). Acute mucosal reactions were scored using Dische system. The supportive anti-inflammatory treatment was given when the severity score exceeded 10.

**Results:** Ninety five patients complied to the assigned treatment. Two patients in the p-CAIR and 1 in the p-CF arm received <60 Gy because of deteriorating general performance and/or tumor progression; one patient died before radiotherapy was started, and one terminated radiotherapy due to psychosis. The average maximum Dische score in both arms of the trial was 11.9 (range 2-21) and was significantly higher in patients treated with p-CAIR, compared to p-CF (10.8 vs. 13.3, p<0.05). Patients with cancer of the oral cavity and oropharynx had higher average maximum Dische scores (p-CAIR:16.4 vs. p-CF:12.3) compared to cancer of the larynx or hypopharynx (p-CAIR:11.8 vs. p-CF:9.6). The average body weight loss during radiotherapy was the same in both arms of the trial (3.3%), but it varied depending on primary tumor site (2.7% larynx/hypoharynx vs. 4.4% other). The hematological toxicity was mild and similar in both arms of the trial. No consequential side toxicity of radiotherapy was observed.

**Conclusions:** The acute normal tissue morbidity in the initial group of 48 patients randomly assigned to the p-CAIR schedule appears acceptable, and allows further recruitment into the trial. In both trial arms patients with cancer of the larynx or hypopharynx tolerated postoperative radiotherapy better than patients with cancer of the oral cavity or oropharynx.

## 2101 Risk Factors and Dose-Effect Relation for Osteoradionecrosis of the Mandible in Oral and Oropharygeal Cancer

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**Purpose/Objective:** To analyze risk factors and dose-effect relation for osteoradionecrosis (ORN) of the mandible following radiotherapy in oral and oropharygeal cancers.

**Materials/Methods:** From 1990 to 2000 one hundred ninety-eight patients with oral (89 patients, 45%) and oropharyngeal cancer (109 patients, 55%) who received external radiotherapy were retrospectively reviewed. The median age was 58 years, and the male-to-female ratio was approximately 4:1. Fourteen (7%), 26 (13%), 29 (15%), and 129 patients (65%) had stage I, II, III, and IV, respectively. Twenty patients (10%) had mandibular invasion by tumor. Of fifty-nine patients (30%) who had mandible surgery 8 patients had partial mandibulectomy, 11 segmental mandibulectomy, 8 lateral mandibulotomy, and 32 median or paramedian mandibulotomy. Fifty-four patients (27%) had induction chemotherapy. All patients underwent dental examination and treatment before radiotherapy. Useful dental findings were obtainable for 138 patients, of which eighty-two patients (59%) had dental extraction. External radiotherapy was performed using Co-60 (69 patients, 35%) or 4 MV X-ray (129 patients, 65%). The median radiation dose was 60 Gy (range 16-75 Gy) and median BED(Gy2) was 114 Gy2 (range 30-167 Gy2).

**Results:** The overall incidence of ORN was 6.6% (13 patients). Of the 59 patients with mandible surgery, 8 patients (14%) had ORN at the site of surgery. Among 139 patients without mandible surgery, 5 patients had ORN (4%) in the molar area of the mandible. The median time to ORN was 22 months after radiation therapy (range 1-69 months). In univariate analysis for risk factors of ORN, the mandible surgery was a significant factor (p=0.01). Logistic regression did not show a positive dose-effect relation (p=0.29) However, radiation dose over BED 106 Gy2 (tumor dose 54 Gy) was a significant factor (p=0.008). In multivariate analysis, the mandible surgery was the most important factor (p=0.001). We performed subgroup analysis in patients with mandible surgery according to surgical procedure. In univariate analysis, BED 106 Gy2 (p=0.002), lateral mandibulotomy (p=0.013), and Co-60 (p=0.045) were proved to be significant risk factors. In multivariate analysis, lateral mandibulotomy (p=0.023) was the most significant factor and radiation dose (p=0.042) was significantly correlated to ORN.