956 POSTER DISCUSSION

Enhanced tumor response and sphincter preservation with preoperative chemoradiation (CXRT) using capecitabine for locally advanced rectal cancer

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Purpose: The objective of this study is to evaluate whether the combination of capecitabine and preoperative radiation (RT) can enhance antitumor and sphincter preservation effect in rectal cancer.

Methods: Locally advanced mid or lower rectal cancer patients without distant metastasis were treated with preoperative CXRT using capecitabine (n=32) or conventional Mayo regimen (n=44). Preoperative RT was delivered to the whole pelvis at 45 Gy followed by a boost of 5.4 Gy to the primary tumor in conjunction with chemotherapy of 2 cycles of capecitabine (2500 mg/day for 2 weeks) and leucovorin (30 mg/day for 2 weeks, PO). For Mayo regimen, 2 cycles of 5-FU (500 mg/m2/day 1-5, IV) and leucovorin (20 mg/m2/day 1-5, IV) were employed. Definitive surgery was performed 6 weeks following completion of preoperative CXRT.

Results: Pathologic complete response (CR) in surgical specimen was achieved in 31.3% of capecitabine group, and in 4.5% of Mayo regimen group (p=0.007). According to Ohboshi-Shimosato's classification, grade III (no viable tumor cells in primary tumor) response was significantly increased in capecitabine group compared to Mayo regimen group (37.5% vs 4.6%, respectively, p=0.001). Downstaging of the depth of the primary tumor and nodal status were markedly increased in capecitabine group ($p<0.01$). The incidence of sphincter preservation for the tumor located less than 6 cm was significantly higher in capecitabine group (90.6% vs 63.6%, p=0.003). Grade 3-4 leukopenia and radiation dermatitis were not found while mild hand-foot syndrome (grade 1-2) was evident in 37.5% in capecitabine group. There was no difference in postoperative complications.

Conclusion: These results suggest that preoperative CXRT using capecitabine may be a very safe, more tolerable and more effective neoadjuvant modality which may increase the chance for sphincter preservation for locally advanced rectal cancer (Supported in part by Roche Korea Co.).

957 POSTER DISCUSSION

The reduction of the operative mortality has improved the overall survival of colorectal cancer in France. A population-based study

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Aim: To estimate changes in factors associated with operative mortality after colorectal cancer surgery over a 20-year period and its consequences on the survival.

Patients: 4,745 new cases of colorectal adenocarcinoma were registered between 1976 and 1995. Among them 84% were operated on and 78% were resected.

Results: Overall operative mortality decreased from 17.7 to 8.1% between 1976-79 and 1992-95. Corresponding rates after curative surgery were 12.6% and 6.2%, respectively. Period of diagnosis, age, sex and subsite were factors independently associated with operative mortality. By applying the operative mortality rates of the 1976-79 period to the 1992-95 period patients, the expected 5-year survival after curative surgery would have been 40% compared to an observed survival of 51%. It corresponds to a 52% relative reduction of operative deaths with an estimated improvement of 27.5% in 5-year overall survival. The application of this results to the French population permits to estimate that 3,000 deaths are annually avoided in France because of the reduction of the operative mortality.

Conclusion: The reduction of operative mortality, due to the progress in surgical techniques and perioperative care, came along with a significant improvement of the survival after curative surgery.

Radiotherapy

958 POSTER DISCUSSION

IMRT versus conventional 3D-CRT on prostate and normal tissue dosimetry using an endorectal balloon for prostate immobilization

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Purpose: To compare prostate and normal tissue dosimetry in prostate cancer patients treated with Intensity Modulated Radiation Therapy (IMRT) versus conventional three dimensional conformal radiotherapy (3D-CRT) using an endorectal balloon for prostate immobilization.

Materials: Ten prostate cancer patients were studied using both IMRT and conventional 3D-CRT at Houston VAMC. Prostate immobilization was achieved with an endorectal balloon inflated with 100 cc of air. For IMRT the prescription was 70Gy at 2 Gy/fraction at the 85% isodose line, allowing no more than 15% of the rectum and 33% of the bladder to receive above 68 and 65Gy, respectively. For conventional 3D-CRT, a six-field arrangement with lateral and oblique 45 degree fields was used to deliver 76Gy at 2Gy/fraction at the isocenter, ensuring complete tumor coverage at the 95% isodose line. Dose volume histograms were generated and dose statistics were compared using the paired Students T-test.

Results: Mean doses for prostate and seminal vesicles were 75.10 and 75.11Gy for IMRT and 75.39 and 75.02Gy for 3D-CRT, respectively ($p>0.218$). Compared to 3D-CRT, IMRT delivered significantly higher maximum doses to prostate and seminal vesicles (by 5.97 and 4.63Gy, respectively, $p<0.001$), but lower minimum doses (by 10.12 and 3.8Gy, respectively, $p<0.001$). 3D-CRT delivered significantly higher doses to 33%, 50% and 66% volumes of rectum by 3.02, 6.64 and 10.09Gy, respectively ($p<0.012$), and upper rectum by 7.47, 9.86 and 9.38Gy, respectively ($p<0.007$). For bladder, marginally higher doses were observed with 3D-CRT to 33% and 66% volumes by 6.71 and 3.37Gy, respectively. Higher doses to femur volumes of 10%, 33% and 50% by 3.56, 9.40 and 9.48Gy, respectively, ($p<0.032$) were also observed with 3D-CRT. Differences in the percent volumes of normal tissues exceeding prescription limits (68Gy for rectum and 65Gy for bladder) were not significant.

Conclusion: This is the first study to assess target and normal tissue dosimetry of IMRT versus 3D-CRT using an endorectal balloon for prostate immobilization. It is shown that IMRT achieves superior normal tissue avoidance especially for rectum and femurs compared to 3D-CRT, with comparable target dose escalation. Clinical studies are currently under way evaluating the impact of IMRT and 3D-CRT in tumor control and normal tissue complication probability.

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Positron emission tomography (PET) image registration into 3-dimensional radiotherapy treatment planning for lung cancer alters computed tomography (CT)-defined tumor and treatment volumes

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Objectives: Conventional thoracic radiation is associated with local recurrence up to 70% in lung cancer. 2D radiation is limited by poor tumor targeting. 3D radiation provides improved targeting by direct transfer of anatomic data into the planning process. PET is a biological imaging tool that provides a spatial map of glucose utilization, which may reflect tumor proliferation, clonogenic density, viability or differentiation, which may influence radiation ports. This study compares the tumor and irradiated volumes from CT-defined anatomical versus PET/CT-defined bioanatomical-based 3D radiation treatment planning.

Methods: Pretreatment CT and PET studies were obtained in treatment position for 12 patients with lung cancer receiving radiotherapy. PET images were registered onto planning CTs. Two 3D treatment plans were generated for each patient using the Planning UNC system. Radiation fields were defined using the anatomic tumor volumes identified by CT, or the bioanatomic tumor volumes based on fusion of PET/CT. DVHs for tumor and normal tissue were calculated using both plans. The gross tumor volume (GTV),

total irradiated volume and percent lung receiving 20 Gy (V20) for the 2 plans were compared.

Results: Incorporation of PET data into planning resulted in 1.2-5.5 increase in GTV for 11 patients, and 0.5 decrease for 1 patient, allowing differentiation between tumor and atalectasis. Unsuspected mediastinal disease was identified in 4(30%). Radiation ports were altered to provide more adequate coverage of the bioanatomic tumor volume in 8 patients. Despite the mean GTV was 2.8 times greater using PET, average increases in total volume irradiated and V20 were only 30% and 20%. Radiation ports were not changed in 2 patients, and were reduced in 2 patients resulting in 17 to 34% decrease in volume irradiated and V20.

Conclusions: Co-registration of PET with planning CT images provides a bioanatomic target that improves delineation of the tumor by better defining extent of local disease and including positive lymph nodes that may not be apparent using CT alone. Incorporation of PET images into treatment planning reduces the likelihood of geographical misses, which may result in improved local control and survival. This information can further assist 3D treatment planning to customize conformal fields so a greater extent of disease can be treated while minimizing the total volume irradiated and V20, and reducing the risk of toxicity.

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Target volume definition in non-small cell lung cancer using 3-dimensional image registration of pre- and post-chemotherapy CT scans

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Aim: Inter-clinician variations in delineating target volumes are a source of systematic errors in radiotherapy treatment planning (RTP). We compared the results of visual transfer of contours to RTP scans with transfer after 3D image registration, in patients receiving induction chemotherapy for non-small cell lung cancer (NSCLC).

Materials and methods: Pre-chemotherapy diagnostic CT scans (on a curved couch-top) and RTP scans (hard couch-top and arm-rest) were performed in 5 patients who received induction chemotherapy, followed by 'involved-field' radiotherapy. A second RTP scan was performed after chemotherapy, and pre-chemotherapy gross tumor volumes (GTV) were reconstructed at an ACQSIMTM workstation by 3 clinicians in the following manner: (i) a 'GTV-visual' generated while viewing the hard copies of the diagnostic CT scan, (ii) a 'GTV-match' after on-screen registration of pre- and post-chemotherapy RTP scans and (iii) GTV's after registration of the pre-treatment diagnostic CT scans with the post-chemotherapy RTP scan. Image registration was performed using the contoured body of a thoracic vertebra adjacent to the tumor. The 'GTV-match' was used for the actual treatment planning. Data were analysed using Cadplan and reproducibility of the contoured GTV's was defined by the ratios of common areas of overlap for the respective contours.

Results: The best method of image registration, as assessed both by clinicians and by ACQSIMTM software was achieved using pre-chemotherapy RTP scans. GTV's derived with 3D image registration were almost invariably larger than those derived using visual contouring (57.4±10% versus 70.8±7%, mean±1SD). Similarly, the mean reproducibility of contouring per patient improved from 61±15.6% to 71.7±9.4% with 3D registration.

Conclusions: 3D image registration of pre- and post-chemotherapy RTP scans resulted in the generation of larger, and more reproducible, GTV's than that derived using visual matching. This technique may be even more important for highly chemosensitive tumors such as small cell lung cancer. The resulting improvement in target volume coverage is likely to improve local tumor control.

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Preservation of salivary function by IMRT: importance of PTV-CTV margin

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Purpose: Xerostomia has a major impact on quality of life after radiotherapy for head and neck tumours. We investigated to what extent the size of the margin between CTV (clinical target volume) and PTV (planning target volume) influences the prospects of modulating the intensity of the beam (IMRT) to preserve parotid gland function.

Methods: For definition of CTV we used a planning CT-scan in a patient treated with primary radiotherapy for oropharyngeal cancer (T2N0). We delineated the CTV for the primary tumour (gross target volume + 1 cm margin for microscopic disease) and the regional node levels II-IV bilaterally. We developed a class solution using IMRT (ITP, PLATO) inverse planning, with 7 beams and 15 intensity levels per beam. The NTCP (normal tissue complication probability) for <25% of the initial parotid gland function was calculated, using IMRT plans, with a margin between CTV and PTV in a range of 0-10 mm. NTCP values of parotid function were derived from our detailed parotid salivary flow measurements in 108 patients treated for head and neck malignancies.

Results: The NTCP for contralateral parotid function was <10% for a PTV-CTV margin of 6 mm or less, 25% for a margin of 8 mm, and 31% for a margin of 10 mm. The NTCP for ipsilateral parotid function was 20% for a margin of 4 mm or less, 31%, 38% and 65% for a margin of 6, 8, and 10 mm, resp.

Conclusion: The uncertainty margin between CTV and PTV, necessary for setup-errors and movement of the patient in the mould, is crucial for the prospects of IMRT to preserve parotid function. Measurements should be taken to keep the margin within 6 mm.

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ESTRO/ASTRO consensus statement on the measurement of metastatic bone pain in radiotherapy trials

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Background: A total of 11 randomised phase III trials, each involving over 100 patients, have addressed the question of optimal fractionation for the treatment of metastatic bone pain. Review of these trials has shown wide variation in the methods used to measure bone pain. The impact of this is highlighted in the analysis of the Dutch bone pain trial reporting a complete response rate of 25% with a pain score of zero, 12% when analgesic use is included and only 4% if global quality of life is used. Across studies wide variation is also seen with the additional impact of differing patient populations

Method: A consensus initiative was established under the auspices of ESTRO and ASTRO in July 2000 to evaluate the various endpoints used and establish a consensus position for definition of pain scoring in future trials of palliative radiotherapy. The first round of discussions held at ASTRO 2000 was based on a questionnaire completed by 35 prominent investigators in the field of metastatic bone pain.

Results: This showed that in some areas of pain assessment there was a clear majority consensus, for example in the use of patient rather than physician scores, the use of a 10 point categorical scale and the use of analgesics as at least a secondary end-point. Other areas identified wider variation and uncertainty, for example definition of partial response, the most appropriate pain to measure, analgesic scoring and impact of retreatment. A second round questionnaire is underway addressing more specific issues within these uncertain areas on the basis of which a consensus statement will be formulated for presentation and approval at the annual ESTRO and ASTRO meetings in Autumn 2001.

Gynaecological cancer

963 POSTER DISCUSSION

Retrospective study of the impact of taxol/platinum (TAX-P) vs non-taxol/platinum (NOTAX-P)chemotherapy on response and survival of patients with advanced ovarian cancer (AOC). Report from a single institution

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Objective: To evaluate if taxol-platinum chemotherapy has improved the outcome of patients (p) with AOC treated in a single institution.

Patients and Methods: Retrospective study. From 1986 to 2000, 190 pt with AOC received platinum-based chemotherapy (64.7% NOTAX-P, 35.3% TAX-P). Characteristics of the p were (NOTAX-P vs TAX-P): mean age: 56 vs 58 y, at least surgical biopsy: 85% vs 82%, FIGO III/IV stages: 79%/21% vs 77%/23%, residual disease >2 cm: 84% vs 80%, 2nd laparotomy: 42%