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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.).

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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

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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),