

difference in grade 3 or higher toxicity. Based on this result, patient should undergo sufficient chemotherapy in combination with radiotherapy to improve pathologic outcome and maximize the chance of sphincter preservation.

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POSTER

Lymphatic mapping and lymphatic endothelial cell isolation in colorectal cancer patients

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Background: Sentinel Lymph Node (SLN) biopsy has already been established as a common procedure, and its clinical usefulness has been confirmed in patients with malignant lymphoma and breast cancer. In colorectal cancer, however, the application of the SLN theory remains uncommon and its clinical significance is also unclear. In addition, the characteristics of the lymphatic vessels that connect SLNs or the lymphatic endothelial cells have been unclear until now. Our purpose is to determine the feasibility and accuracy of SLN mapping by intraoperative subserosal dye injection and to develop a novel method for the isolation of anatomically defined lymphatic endothelial cells.

Methods: SLN biopsy by the subserous dye injection method (patent blue) was conducted in 36 patients with colorectal cancer for which curative resection was possible (stage 0: 2 cases, stage I: 18 cases, stage II: 4 cases, stage III: 12 cases), with additional systematic lymph node dissection. Lymphatic endothelial cells were isolated from lymphatic vessels identified at the time of the SLN biopsy by the collagenase II perfusion method, and we tried to transfer them into a culture system with an endothelial cell-specific medium and evaluated the biological properties of the isolated cells using molecular procedures.

Results: SLNs could be identified in 34 cases (94%). The total number of resected lymph nodes was 705, and 72 of those nodes were confirmed as SLNs (10.2%). Ten metastasis-positive nodes were found in SLNs (13.9%), and the mean number of identified SLNs per case was 2.0. The sensitivity to detect metastatic lymph nodes and the specificity of the SLN biopsy for all removed lymph nodes was 86.1% and 99.2%, respectively. No complications or toxicity associated with the dye injection were observed. In addition, cells isolated from removed lymphatic vessels formed colonies with endothelial cell-specific properties, and the expression of lymphatic endothelial cell-specific markers, VEGFR-3, Podoplanin and Prox-1 was observed.

Conclusion: The SLN biopsy by the dye method for colorectal cancer is a procedure with high sensitivity, accuracy and safety that is applicable to cases with advanced cancer. In addition, a method was established to isolate only lymphatic endothelial cells from resected lymphatic vessels and to culture them. Our results are expected to be another milestone in the determination of the rational margin of resection in colorectal surgery and the future clarification of the mechanism of lymphatic metastasis.

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POSTER

Comparison of CT-guided and PET-CT guided radiotherapy planning in patients with rectum cancer treated preoperatively

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Background: Positron emission tomography (PET) has a potential improvement for staging and radiation treatment planning of various tumor sites. We analyzed the use of 18F-fluorodeoxyglucose (FDG)-PET/computed tomography (CT) images for gross tumor volume delineation of patients with rectum carcinoma candidates for preoperative conformal radiotherapy.

Materials and Methods: Twenty seven patients with rectum cancer for preoperative radiotherapy had both CT and PET images acquired. For each patient Gross Tumor Volume (GTV) was contoured on CT (CT-GTV) and PET/CT images (PET/CT-GTV). The volumes of CT-GTV and PET/CT-GTV were compared, also the intersection volumes, and tumor volumes remained outside PET/CT and CT were compared.

Results: The PET/CT-GTV ($48.5 \pm 8.5 \text{ cm}^3$) was significantly greater than the CT-GTV ($30 \pm 5.6 \text{ cm}^3$) ($p = 0.002$), respectively. The mean difference between PET/CT-GTV and CT-GTV was 38%. The intersecting tumor volume for both methods was $22 \pm 25 \text{ cm}^3$, and tumor volumes remaining outside CT and PET/CT were $24.5 \pm 29 \text{ cm}^3$ and $6.5 \pm 5.5 \text{ cm}^3$ respectively. PET/CT use causes a 38% increase in GTV, which may prevent

unnecessary normal tissue irradiation and may cause geographic miss because of less GTV contoured on CT.

Conclusion: Co-registration of PET and CT information in rectum cancer may improve the delineation of GTV and theoretically reduce the likelihood of geographic misses. Imaging with PET/CT for preoperative radiotherapy of rectal cancer may lead to a change in target volume delineation. The GTV changed significantly, with a mean increase in size of 38%. PET/CT fusion images could have a potential impact on treatment planning.

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POSTER

Helical tomotherapy or intensity-modulated radiation therapy in the treatment of anal cancer: experience of Geneva and Lausanne

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Background: To assess the early clinical outcomes and toxicities in patients treated with high precision radiation therapy (RT) consisting of helical tomotherapy (HT) or intensity-modulated radiation therapy (IMRT) for anal cancer.

Materials and Methods: Since March 2006, 30 patients with stage I-IIIB anal squamous-cell carcinoma were treated curatively by IMRT or HT alone ($n = 2$) or by concomitant chemotherapy and IMRT or HT ($n = 28$). Median age was 59 years (range, 36–83 years) and the female/male ratio was 2.3 (21/9). Primary tumor site was anal canal, anal margin, or both in 26, 1, and 3 patients, respectively. Anal tumor, pelvic and inguinal nodes were irradiated with a median dose of 36 Gy using HT, or 5- or 7-field IMRT in 18 and 12 patients, respectively; After a planned gap of 1–2 weeks (median 1 week), a median boost dose of 23.4 Gy was delivered to the tumor and/or involved nodes using 3DRT ($n = 24$) or HT/IMRT ($n = 6$). The total delivered dose ranged between 59.4 and 64.8 Gy (median, 59.4 Gy). Concomitant chemotherapy consisted of mitomycin C alone ($n = 1$), mitomycin C and 5-fluorouracil ($n = 17$) or capecitabine ($n = 10$) in 28 patients. Common Terminology Criteria for Adverse Events v3.0 scale was used to score acute and late toxicities.

Results: All but one patient, who developed progressive local and distant disease at the end of RT, achieved a complete response. Twelve months following RT, one patient had a recurrence at the primary tumor site, salvaged with brachytherapy. After a median follow-up of 7.5 months (range, 1–35 months), no deaths were observed. The 2-year actuarial locoregional control and probability of disease control without colostomy rates were 82% and 79%, respectively. RT was well tolerated without any unplanned treatment interruptions. Grade 1 or 2 acute adverse events consisted of skin toxicity in 8 and 22 patients, diarrhea in 18 and 3 patients, and cystitis in 9 and 2 patients; respectively. Only one patient developed grade 3 mucosal necrosis at the end of the treatment, requiring diverting colostomy. No difference in terms of acute toxicity was observed between patients treated with HT or IMRT. None of the 22 patients with a follow-up of more than 3 months developed grade 3 or more late toxicity.

Conclusions: Our preliminary results suggest that HT or IMRT combined with concomitant chemotherapy for anal cancer is effective, and associated with favorable rates of toxicity compared with historical series. Further follow-up is warranted to assess late toxicity.

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POSTER

Prognostic value of pathological complete response after neoadjuvant therapy for locally advanced rectal cancer – a monoinstitutional experience

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Background: In the European randomized trials of neoadjuvant CRT the rate of complete response (CR) ranged from 11–16%. A favorable prognosis was observed for CRT after preoperative therapy in patients with locally advanced rectal cancer. The aim of our analysis was to verify whether ypCR predicts a favorable outcome.

Methods: 234 pts with locally advanced low and mid rectal cancer underwent neoadjuvant CRT in our academic institution from January 1998 to December 2007. Eligibility criteria included locally advanced rectal cancer with no distant metastases and evidence of ypCR after CRT. All patients received the same neoadjuvant treatment with 5-FU and Oxaliplatin. After a median interval of 8 weeks after completion of CRT patients underwent a radical resection according to the principles of TME. Standard pathological tumor staging of resected specimen was

performed according to the AJCC Cancer staging Manual. The pCR was defined by no evidence of viable tumour cell on pathologic analysis. Local recurrence was defined as clinical, radiological or pathological evidence of tumour in any other site. The time to last follow up, local recurrence, or death was measured from the time of radical resection. Disease free and overall survival were estimated using the KM method, and differences between survival curves were determined by using the log rank test. A P value of <0.05 was considered statistically significant.

Results: 37 pts had a complete response and 78 pts were not responders. Sphincter preservation, anteroposterior resection and endoscopic surgery were performed in 36 pts (97.2%). A patient with complete refused rectal surgery. Mean number of examined lymphnodes was 14.3 ± 7.95 . Median follow up was 60 months. In pCR pts no locoregional recurrence occurred and distant metastase occurred in 2 pts (5.4%). In the no responder group we found 18 local recurrence ($p=0.0001$) and 46 patients developed distant metastases ($p=0.0001$). The pCR group 5-years overall and disease free survival were 97% and 94% respectively. During the follow up one patient died.

Conclusions: The improved ontological outcome in patients with rectal cancer who achieve a pCR appears related to their significantly decreased rate of distant failure when compared with no down staging patients. To further improve the oncological outcomes and sphincter preservation rates in patients with locally advanced rectal cancer, the molecular mechanism governing the rectal cancer response to preoperative CRT need to be explored.

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POSTER

Randomized phase III trial comparing preoperative versus postoperative radiotherapy with capecitabine in locally advanced rectal cancer

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Background: Preoperative chemoradiotherapy using bolus fluorouracil demonstrated the superiority of preoperative treatment in local control and sphincter preservation in locally advanced rectal cancer. We conducted a prospective, single-institutional, phase III trial which compared preoperative chemoradiotherapy with postoperative chemoradiotherapy using oral capecitabine. We present the final results of our trial in this report.

Materials and Methods: Patients with locally advanced rectal cancer (cT3 or N+) were randomly assigned to receive either preoperative (arm I) or postoperative (arm II) chemoradiotherapy. Preoperative radiotherapy was delivered to the pelvis at a dose of 46 Gy in 23 fractions, followed by a boost of 4 Gy in 2 fractions. Postoperative radiotherapy consisted of 50 Gy in 25 fractions to the pelvis without boost. Capecitabine ($1,650 \text{ mg/m}^2/\text{day}$) was administered concurrently during radiotherapy. Surgery was performed according to total mesorectal excision technique with the time interval of 4–6 weeks in both arms. This protocol was closed earlier than initially planned due to difficulty in patient enrollment.

Results: Between March 2004 and April 2006, 117 and 123 patients were randomly assigned to arm I and arm II, respectively. Clinical characteristics were well balanced between the two arms, except more low-lying ($\leq 5 \text{ cm}$ from anal verge) tumors in arm I (60% vs. 46%, $p=0.041$). In the patients with lower-lying tumors, arm I showed higher rate of sphincter sparing surgery (68% vs. 42%, $p=0.008$). After a median follow-up of 47 months, the 5-year cumulative incidence of local recurrence was non-significantly higher in arm II (3% vs. 6%, $p=0.335$). The 5-year overall survival and disease-free survival rates were not different between two groups. Ninety-nine patients (92.5%) in arm I and 84 patients (74.3%) in arm II completed chemoradiotherapy as planned. Grade 3 or higher acute toxicity was observed in 15% of the patients in arm I and 16% in arm II. Postoperative complications were also similar in both arms.

Conclusions: Preoperative or postoperative chemoradiotherapy with oral capecitabine was safe and well tolerated. Although we could not demonstrate significant benefit of preoperative chemoradiation in local control and survival, our data showed that increased rate of sphincter preservation was possible in lower-lying tumors without jeopardizing local control and surgical complication by preoperative chemoradiotherapy.

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POSTER

The use of the cell saver in rectal cancer surgery is safe

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Introduction: In T4 and locally recurrent rectal cancer the dissection planes often need to be extra anatomically. Blood loss in fibrotic tissue (after prior primary treatment or after recent radiochemotherapy) may be considerable. The use of the cell saver can help to reduce the need for donor blood. In non-oncological procedures the role of the cell-saver has been recognized. However, in oncological surgery the cell saver is being used much less for fear of disseminating tumour cells.

Patients and Methods: Our hospital is a centre for complex rectal cancer surgery. In more than half of the patients blood loss exceeds 2.5 litres. Since more than ten years, the cell saver is used to return filtered and washed erythrocytes to the patient in order to maintain the circulating red cell volume. Since 1994 until December 2006 290 patients have been treated for advanced rectal cancer and the data were collected prospectively. Four quartiles representing the volume of blood loss were created. (Q1 less than 1385 ml (n=69), Q2 1385 up to 2500 ml (n=76), Q3 2500 up to 4650 ml (n=62), Q4 more than 4650 ml n=69)).

Results: Univariate analysis showed that particularly in the largest blood loss quartiles outcome parameters were improved. Cancer specific survival at 5 years for patients in whom the cell saver was used (n=151) per quartile blood loss volume compared to those without cell saving (n=125) were 74%, 85%, 78%, 76% and 73%, 86%, 60%, 30% respectively ($p=0.042$ in Q3 and $p=0.012$ in Q4, overall $p=0.002$). The percentages for metastasis free survival were 74%, 85%, 78%, 76% and 77%, 71%, 71%, and 37% respectively ($p=0.038$ for Q4, overall n.s.). Other significant variables for oncological outcome were: free circumferential margin, lymphnode status, the use of neoadjuvant chemotherapy compared to radiotherapy alone and the use of adjuvant chemotherapy. After multivariate analysis the use of the cell saver did only show a positive trend, unlike the other variables, which remained significant.

Conclusion: Since 1994 the multimodality treatment of advanced rectal cancer has changed. It is difficult to establish the exact role of the cell saver in the oncological outcome of these patients. However modelling of multivariate analysis and stratification for all tumour variables did never show a negative outcome for the use of the cell saver. In all models the trend remained positive. Therefore we conclude, that introduction of the cell saver did not compromise oncological outcome and is safe to use in these kinds of patients.

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POSTER

Robotic radiosurgery in the local control of unresectable liver metastases in patients with colorectal cancer – preliminary results

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Background: The median survival of untreated patients with liver metastases ranges between 6 and 18 months, but unfortunately surgery may be performed in only 20% of cases. The aim of this preliminary study was to evaluate the usefulness of CyberKnife® (Accuray Inc, Sunnyvale, CA) image-guided robotic stereotactic radiosurgery for local control of unresectable liver metastases.

Patients and Methods: Eight-teen consecutive patients with liver metastases from colorectal cancer, considered unsuitable for surgery, confirmed by ultrasound- or CT-guided biopsy or ultrasound-guided FNAB, were enrolled in the study. There were 11 men and 7 women, with an overall median age of 59 years (range 49–73 years). The inclusion criteria were: age between 50–75, no chemotherapy during the last 30 days, acceptable liver function (ALT and ALT<150 U/L, PT >2.5%), Karnofsky performance score <3, no extra-hepatic disease on 18-FDG CT-PET, tumor size and estimated residual liver volume on CT-scan <6 cm and >700 mL, respectively.

Results: The overall tumor volume ranged from 25 to 185 mL (median 70 mL), and the irradiated volume was $18 \pm 10 \text{ mL}$ (range 11–40 mL). The