with 5-fluorouracil protracted venous infusion (300 mg/m^2/day, 5 days/7, during 5 consecutive weeks) and Cisplatinum (20 mg/m^2/day, D1–5 and D 29–33), followed by a complete restaging evaluation 3–4 weeks after chemoradiation. Those without disease progression underwent immediate surgery. This study enrolled, over 4 years, 41 pts (61% men, mean age 59 years (range 33–75), with toxicity and survival data available for 40. Median tumor size was 3.1 cm, 9 pts presented positive nodes at CT scan and/or ultrasonography. All pts completed radiation, 37/41 (90%) received at least 46 Gy, 30/41 (73%) received at least 75% of the chemotherapy dose. Twenty six patients (63%) underwent a curative surgical resection, 6 had a palliative anastomosis, 4 a laparotomy, 5 (12%) did not undergo surgery due to distant disease progression at restaging. Thirty day post-operative mortality was 0.24%. Four patients presented a grade 4 (G4) hematological toxicity, 1 had a G4 postoperative sepsis, 1 died of late sepsis at 2 months post-surgery. Pathological findings show, in 11/26 pts (46%) more than 80% strongly alterated malignant cells, associated with necrotic areas in 72% of cases. One pathological complete response has been described. The feasibility of this preoperative concurrent chemoradiation regimen was established (67.5%); disease progression during the the 9–11 week preoperative period was rare (12%); 63% of all pts underwent a potentially curative resection. Toxicity was manageable and did not prevent successful surgery. This scheme compares favorably to other studies, and can now be tested on a phase III setting. Definitive data will be presented during the meeting.

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Clinical results of inoperable hepatocellular carcinoma treated with three-dimensional conformal radiotherapy: factors affecting the tumor response and survival rate

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Purpose: To evaluate the clinical results of factors affecting tumor response and survival rate of patient with hepatocellular carcinoma (HCC) treated with three-dimensional conformal radiotherapy (3D-CRT).
Materials and methods: From 1998 to 2004, 49 patients (pts) with HCC were treated with 3D-CRT. They were not indicated for surgery. Their characteristics were follows: mean age 68.5 years old (41–85 y.o.); performance status (PS): 35 pts in 1, 12 pts in 2, and 2 pts in 3; Child-Pugh classification: 23 pts in class A, 19 in B, and 7 in C; UICC (2002) stage: 23 pts in II, 27 in III, and 19 in IV. 15 pts had ascites before 3D-CRT. 32 pts were treated for main hepatic tumor, 15 for PV tumor thrombi, and 2 for IVC thrombi. The mean tumor size was 4.3 cm (range 1.3–12 cm). The mean radiation dose was 44 Gy (15–60 Gy) in a daily fraction of 2–3 Gy using 10-MV linear accelerator. The mean biologic effective dose at $\alpha/\beta = 10$ was 44.7 Gy. Tumor response was evaluated by the change in maximum diameter detected on CT and MRI images 1–3 months after radiotherapy. The variability of age, PS, Child-Pugh classification, UICC stage, ascites, PV/IVC tumor thrombi, tumor size and radiation dose was evaluated between complete response (CR) + partial response (PR) group and no change (NC) + progressive disease (PD) group. The factors associated with survival were also evaluated by using Cox regression model. Lesion-to-liver contrast-to-noise ratio (CNR), signal-to-noise ratio (SNR), and standard deviation (SD) were evaluated on T2 weighted MR imaging before and after radiotherapy in 38 patients.
Results: The mean follow-up was 9 months (2–40 months). 16 patients (33%) got PR, 22 (45%) NC, 11 (22%) PD, and no patient got CR. The tumor response rate (CR+PR) was 33%. Radiation dose was the only significant factor for tumor response on Mann-Whitney U-test ($p < 0.05$). The over all survival rate at 1 and 2 year was 49.6% and 24.3%, respectively (median survival 14.5 months). On univariate analysis, PS, Child-Pugh classification, PV tumor thrombi and ascites were significant factors for survival rate ($p < 0.05$). On multivariate analysis, PS was only significant factor. In PR group, CNR after radiotherapy was significantly higher than before ($p < 0.01$).
Conclusions: Radiation dose was significant factor in tumor response, while tumor size and PV/IVC tumor thrombi were not significant. CNR was useful to evaluated tumor response of the patient with HCC treated with 3D-CRT. Additional efforts for dose escalation may be warranted to improve the treatment results.

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Histological results of endoscopic resection for esophageal lesions diagnosed as high-grade intraepithelial squamous neoplasia by endoscopic biopsy

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Background: The ability to detect early squamous neoplasia of the esophagus can be enhanced considerably by iodine staining during endoscopic examination. Histologically, biopsy specimens obtained from the lesion detected in endoscopic screening were often diagnosed as high-grade intraepithelial squamous neoplasia (WHO 2000). However, there are very few reports on the characteristics of such intraepithelial squamous lesions, and a management strategy for such lesions has therefore not been established. In this study, we prospectively performed endoscopic mucosal resection (EMR) for esophageal lesions diagnosed as high-grade intraepithelial squamous neoplasia by endoscopic biopsy and investigated histological features of the lesions in totally resected specimens.
Patients and methods: During the period from April 2001 to September 2004, 51patients were found to have lesions diagnosed as high-grade intraepithelial squamous neoplasia of the esophagus by endoscopic biopsy at Hokkaido University Hospital and associated hospitals. All patients underwent EUS with the use of a high-frequency catheter probe and were confirmed to have no evidence of submucosal tumor invasion. Subsequently, all patients underwent EMR at Hokkaido University Hospital.
Results: Histological examination of totally resected specimens revealed that 12 (23.5%) of the 51 patients had tumor invasion of the basement membrane that was confined to the lamina propria mucosae and that 4 (7.8%) of the 51 patients had tumor invasion of the muscularis mucosae. The remaining 35 patients (68.6%) were confirmed to have high-grade intraepithelial squamous neoplasia of the esophagus. The invasive focus all of the 16 lesions of invasive squamous cell carcinoma was surrounded by high-grade intraepithelial squamous neoplasia.
Conclusions: Histological results suggested that high-grade intraepithelial squamous neoplasia of the esophagus has characteristics of carcinoma in the pre-invasive stage. EMR, which can be employed both therapeutically and diagnostically, should be performed for esophageal lesions diagnosed by endoscopic biopsy as high-grade intraepithelial squamous neoplasia not only because of its probable malignant potential but also because over 30% of such lesions are actually invasive carcinoma.

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Postoperative adjuvant gemcitabine alone and concurrent with radiation after resection of locally advanced pancreatic carcinoma

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Purpose: Gemcitabine is a pyrimidine analogue which has potential activity in advanced pancreatic cancer and is a powerful radiosensitizer. We evaluated the efficacy and toxicity of postoperative administration of Gemcitabine (GEM) alone, followed by concurrent GEM and irradiation (RT) after resection for locally advanced pancreatic adenocarcinoma.
Methods and materials: Between 1999–2004, thirty-three patients (median age 58 years, range 21–78, median Karnofsky Performance Status 90, range 70–100) with stage II (7 patients) and stage III (26 patients) resected pancreatic adenocarcinoma were treated. Twenty-nine patients (88%) had RO and four patients (12%) had R1 resection. GEM 1000 mg/m^2 on D1, 8, 15 was given within a median of 32 (range 21–103 days) days after surgery, followed by GEM 300 mg/m^2 weekly concurrent with radiotherapy (50.4 Gy in 180 cGy daily fractions(. After the completion of chemoradiotherapy, patients received three additional courses of GEM 1000 mg/m^2 on D1, 8, 15 in one cycle. Each cycle consisted of 3 weeks of treatment followed by a 2 week chemotherapy free interval.
Results: Twenty-four (73%) patients received 4 to 6 courses of weekly GEM, eight patients received 2 to 3 courses and one patient could not receive any. Grade III-IV hematologic toxicity, mainly leuocopenia occurred only in 3 (9%) patients. Grade I and II gastrointestinal toxicity (nausea, vomiting) occurred in 9 patients (27%), whereas grade III or IV gastrointestinal toxicity was not observed. Concurrent gemcitabine and radiotherapy was completed without treatment interruptions in 33% of the patients. Median treatment interruption was 3 days (range 1–26 days). Twenty-seven patients (81.8%) received GEM after chemoirradiation. During a median follow-up of 35 months (range, 12–68) local recurrence was observed in 4 (three of them had peritoneal seeding or distant