P-01  Efficacy of staged treatment strategy for patients with synchronous double cancers of the esophagus and head and neck

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Objective: To determine whether a staged treatment strategy is acceptable for patients with synchronous double cancers.

Background: Synchronous occurrence of esophageal and head and neck (H&N) cancers is frequently observed.

Methods: We retrospectively reviewed the records of 109 patients with synchronous double cancers of the esophagus and H&N treated between 2005 and 2011. Fifty-one patients underwent synchronous treatment and 58 underwent staged treatment. We measured the delay in treatment for the second cancer in the staged treatment group and evaluated how many patients experienced progression of the second cancer during the first cancer treatment. Overall survival (OS) was analyzed in 100 patients who underwent potentially curative treatment.

Results: Synchronous treatment strategy was frequently selected for patients with both advanced cancers (77%) compared with those who had early cancers in either or both organs (43%) (P=0.02). The median delay in the treatment for the second cancer was 80 days; 77.5 days in the H&N-first group and 96 days in the esophagus-first group. Only one patient experienced stage progression during the waiting period. There was no significant difference in OS between the synchronous treatment group and the staged treatment group (P=0.73), and no significant difference in OS among patients who had advanced cancer in the H&N, esophagus or both.

Conclusions: Prognosis of patients with synchronous cancers depends on that of the more advanced cancer, and waiting for treatment of early cancers may not influence survival. The staged treatment strategy is acceptable when either of the double cancers is at an early stage.


P-02  Prognostic and clinical impact of sarcopenia in esophageal squamous cell carcinoma

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Background: Recently, depletion of skeletal muscle mass (sarcopenia) has been linked to poor prognosis in several types of cancers, but has not been investigated in esophageal squamous cell carcinoma (ESCC). This retrospective study investigates the relationship between sarcopenia and clinical outcome in ESCC patients treated by surgical resection or definitive chemoradiation therapy (dCRT).

Methods: The study was conducted in a single academic hospital in Kumamoto, Japan, and involved 325 ESCC patients (236 surgical cases and 69 dCRT cases) treated between April 2005 and April 2011. The skeletal muscle tissue areas (psoas, paraspinal muscles and abdominal wall muscles) were measured by the SYNAPSE VINCENT system. Initial cancer staging was performed on CT scans taken within 4 weeks of treatment initiation. The evaluated samples were slices of the third lumbar vertebrae (L3) in the inferior direction. The muscle area normalized by the square of the height (m^2/m^2) is called the skeletal muscle index (SMI) (cm^2/m^2).

Results: SMI in the 325 ESCC patients was distributed as follows: mean: 47.10; median: 46.88; standard deviation (SD): 7.39; range: 31.48-71.11; interquartile range, 46.29-47.90. Skeletal muscle tissue was greater in male patients than in female patients (p < 0.0001), but was independent of other clinical and tumor features. Third tertile SMI group (T3; < 44.5 cm^2/m^2 for male patients, < 36.5 cm^2/m^2 for female patients) was defined as the “sarcopenia group.” Sarcopenia was not significantly associated with overall survival (log rank p = 0.54). Lymph node involvement significantly altered the relationship between sarcopenia and survival rate (p for interaction = 0.029). Sarcopenia significantly reduced the overall survival of patients without lymph node involvement (log rank p = 0.035), but was uncorrelated with overall survival in patients with lymph involvement (log rank, p = 0.31). Moreover, as concerns short-term surgical outcome, the anastomosis leakage rate was significantly higher in the sarcopenia group than in the non-sarcopenia group (p = 0.032), but other surgical complications did not significantly differ between the two groups.

Conclusions: Sarcopenia in ESCC patients without lymph node involvement is associated with poor prognosis, indicating sarcopenia as a potential biomarker for identifying patients likely to experience an inferior outcome. Moreover, sarcopenia was associated with anastomosis leakage but no other short-term surgical outcome.
P-03  Lysine-specific demethylase-1 contributes to malignant behavior in esophageal cancer

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Background: Esophageal cancer is the eighth most common cancer and the sixth leading cause of cancer mortality. Despite remarkable advances in multimodal therapies, the prognosis of esophageal cancer patients remains poor even after complete resection. To assess the range of tumor progression and predicting prognoses of esophageal cancer, 18F-fluorodeoxyglucose position emission tomography (FDG-PET) has become available. As FDG-PET can also detect the glucose uptake of cancer cells, it suggests a close relationship between cancer metabolism and malignancy in esophageal cancer. Lysine-specific demethylase-1 (LSD1) removes the methyl groups from mono- and di-methylated lysine 4 of histone H3, and previous studies demonstrated that LSD1 had a crucial role on malignancy in several human tumors. Moreover, LSD1 is considered to epigenetically regulate the energy metabolism genes in adipocytes and hepatocellular carcinoma. We investigated the function of LSD1 in the invasive activity and the metabolism of esophageal cancer cells.

Materials and Methods: We investigated the relationships between LSD1 immunohistochemical expression levels, clinical and pathological features, including the SUVmax (maximum standard uptake value) in FDG-PET assay. The influence of LSD1 on cell proliferation, invasion and glucose uptake was evaluated in vitro by using specific small interfering RNA for LSD1 (siLSD1) and an LSD1 inhibitor. We also evaluated two major energy pathways (glycolytic pathway and mitochondrial respiration) by measuring the extracellular acidification rate (ECAR) and the oxygen consumption rate (OCR) with an Extracellular Flux Analyzer.

Results: High LSD1 immunohistochemical expression was significantly associated with high tumor stage, lymphovascular invasion, and high SUVmax in esophageal cancer patients. In addition, in the Kaplan-Meier analysis, overall survival time was significantly shorter for patients in the high LSD1 group than for their low group counterparts (5-year survival rate 65.4% vs. 91.4%, log rank p = 0.0017). The disease-free survival time was also significantly reduced for these patients (3-year survival rate 90% vs. 82.7%, log rank p = 0.023). In the in vitro analysis, LSD1 knockdown significantly suppressed the invasive activity, but not proliferation. Moreover, LSD1 knockdown significantly suppressed glucose uptake of cancerous cells. Reduced their ECAR and increased their OCR/ECAR.

Conclusion: LSD1 may contribute to malignant behavior by regulating the invasive activity and metabolism, activating the glycolytic pathway and inhibiting the mitochondrial respiration of esophageal cancer cells. These mechanisms could be exploited in cancer therapeutics. Future studies are needed to confirm our findings, and to examine other potential mechanisms by which LSD1 affects tumor behavior.

P-04  Oncological significance of modified Clavien classification for the complications after esophagectomy for cancer

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Background: Modified Clavien classification is a simple, reproducible, and commonly used grading system for postoperative complications. Oncological significance of severity of the complications after esophagectomy for cancer is not fully understood. We aim to clarify the impact of postoperative complications after esophagectomy on oncological prognosis in patients with esophageal cancer when using modified Clavien classification.

Patients and Methods: A total of 516 consecutive patients who underwent curative esophagectomy for thoracic esophageal cancer between 1985 and 2008, excluding patients with postoperative mortality, were enrolled in this study. Patients were divided into three groups according to the maximum grade of postoperative complications as follows: Group A (none or grade I, n = 288), Group B (grade II, n = 131) and Group C (grade III or higher, n = 97). Clinicopathological characteristics, surgical procedures, recurrence free survival (RFS), and disease specific survival (DSS) of the three groups were retrospectively analyzed. The Cox proportional hazard model was used to identify the independent prognostic factors for RFS and DSS.

Results: Postoperative complication occurred in 349 patients (67%). Clinicopathological characteristics were not significantly different among the three groups. Transhiatal esophagectomy and colonic reconstruction were most frequently performed in Group C (P < 0.01 and P = 0.02, respectively), and the number of dissected nodes was highest in Group C (P = 0.04). Operative time and the length of postoperative hospital stay were significantly longer in Group B and C than in Group A (P < 0.01 and P < 0.01, respectively). Five-year RFS in Group A, B and C were 62%, 56% and 55%, respectively. The presence of grade III or higher complications significantly and unfavorably affected the RFS (adjusted hazard ratio, 1.70; 95% confidence interval, 1.13-2.54; P = 0.011). Significantly fewer patients received anti-cancer treatments after recurrence in Group C (40%) than in Group A (60%) or Group B (68%), (P < 0.01). Five-year DSS in Group A, B and C were 66%, 66% and 59%, respectively. The presence of grade III or higher complications was significantly unfavorable prognostic factor for DSS (adjusted hazard ratio, 1.54; 95% confidence interval, 1.02-2.32; P = 0.04).

Conclusions: Severe complications after esophagectomy classified as Grade III or higher of modified Clavien classification is an independent risk factor for postoperative recurrence in esophageal cancer. Furthermore, the DSS in patients with severe complications might be unfavorable because of missing an opportunity for anti-cancer treatments after recurrence.
P-05  Relationship between high-resolution manometry and timed barium esophagogram findings in patients with achalasia

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Aim: The aim of this study was to investigate the relationship between high-resolution manometry (HRM) and timed barium esophagogram (TBE) findings.

Methods: A retrospective review of a prospectively maintained database was conducted to identify patients with achalasia who underwent HRM and TBE before surgery between November 2013 and December 2014. Patients who had previous surgery and/or who were diagnosed to have type III achalasia were excluded.

Results: Thirty-one patients met the inclusion criteria (mean age 42.5 ± 15.9 years, 16 female). Eleven patients (35%) had type I achalasia and the other 20 patients (65%) had type II achalasia on HRM findings. Breakdown of morphologic type on TBE was as follows: Straight type, n=23; and Sigmoid type, n=8. The severity of dilatation consisted of grade I in 6 (19%), grade II in 18 (58%), and grade III in 7 (23%). There were no significant correlations in the morphologic type and the severity of dilatation on TBE between type I and type II achalasia (p=0.124 and p=0.522, respectively). However, patients with type I achalasia had wider esophagus compared with those with type II achalasia (p=0.004). Significant correlations were identified between integrated relaxation pressure and the morphologic type (p=0.042), and Lower esophageal sphincter pressure integral and the morphologic type (p=0.033), respectively. Besides, significant negative correlations were present between the number of panesophageal pressurization out of 10 wet swallows and width of esophagus on TBE (p=0.014).

Conclusion: There was a significant negative correlation between body function on HRM and the severity of esophageal dilatation on TBE.

P-06  Predictive factors related occurrence of pancreatic fistula and its aggravation after radical gastrectomy for gastric cancer

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Background
Pancreatic fistula (PF) and subsequent intra-abdominal abscess is a serious complication after gastrectomy for gastric cancer (GC). Insertion of drainage tubes at the time of gastrectomy could be useful for the prediction of such complications by measuring the amylase concentration of drainage fluid (d-AMY). The objective is to analyze the predictive factors related PF and its aggravation after gastrectomy by means of perioperative clinical information that includes not only d-AMY but C-reactive protein (CRP) in the serum chemistry.

Methods
463 patients underwent gastrectomy for GC at our department were analyzed. Closed drains were placed in the left subphrenic cavity and Winslow’s cavity of the patients treated with total gastrectomy (TG), in the left subphrenic cavity of those treated with proximal gastrectomy (PG), and in Winslow’s cavity of those treated with other types of gastrectomy. The d-AMY was measured on the first, third, and fifth postoperative days along with the serum chemistry. The patients' postoperative course was followed closely and recorded, and correlation between the incidence of PF-related intra-abdominal abscess and d-AMY level on the first postoperative day was evaluated. CRP level was also focused on whether it might indicate the PF-related complication throughout the postoperative period.

Results
TG was performed in 127 patients, PG in 23, distal gastrectomy (DG) in 277. PF, diagnosed in 58 (12.9%) patients, was stratified according to Clavien-Dindo (CD) classification, as a result of which grade I PF was found in 15, grade II in 11 and grade III which includes PF-related abscesses that was managed by replacement of a drainage tube inserted during surgery by a new tube in 32 patients. The cutoff value of d-AMY on the first postoperative day for predicting the grade III PF was 1949 IU/l. The cutoff value of serum CRP level on the third postoperative day for the same purpose was 20.44 mg/dl. Assessment by linear mixed model revealed that, in patients who had PF-related abscess, relatively high CRP levels were maintained even after the third postoperative day compared to those with CD grade I / II PF. Multivariate analysis demonstrated that d-AMY and serum CRP were predictive factors for grade III PF.

Conclusions
The d-AMY on the first postoperative day and serum CRP on the third postoperative day might be useful for predicting occurrence of PF and subsequent intra-abdominal abscess after gastrectomy.
**P-07**  
**Perforation of the portal vein due to duodenal ulcer: A case report**  
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**Background:** Perforation of the portal vein due to duodenal ulcer is extremely rare, and only 5 such cases have been reported in the literature.

**Case:** A 59-year-old man was admitted to the emergency room with hematemesis, melena and general malaise. His hemoglobin was 6.2 g/dl for which he required transfusion of 8 U of packed red blood cells. He immediately underwent upper gastro-intestinal endoscopy, in which hemorrhagic ulcer was identified at the posterior wall of the duodenal bulb, which was controlled by endoscopic hemostasis. Abdominal CT showed irregular wall swelling of the antrum of the stomach and the duodenum, and portal vein thrombosis (PVT) with gas in the portal vein. The next day, he underwent repeated upper gastro-intestinal endoscopy for progressive anemia, which failed to control the hemorrhage due to poor visibility by active bleeding. Subsequently, transarterial embolization was attempted, which failed to demonstrate extravasation. On the same day, due to persistent bleeding, the patient underwent emergency surgery. In order identify the source of bleeding directly, the anterior wall of duodenum was incised, when rapid venous hemorrhage was encountered. Due to low visibility caused by bleeding, we identified the location of the ulcer by palpation. Hemorrhage was controlled by pressing the ulcer floor by fingers and perforation of the portal vein due to duodenal ulcer was confirmed. The size of the perforated lesion was approximately 1.5 cm in diameter. The lesion was temporarily suture-obliterated by surrounding tissues, and distal gastrectomy with Roux-en-Y reconstruction and jejunostomy were performed. Duration of the operation was 281 min, and the intraoperative blood loss was 4,170 ml for which 18 U of packed red blood cells were transfused during the operation. Immediately after the operation, liver failure due to shock liver developed, and the patient died on postoperative day 12.

**Conclusion:** We experienced an extremely rare case of perforation of the portal vein by duodenal ulcer.

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**P-08**  
**Unexpected small bowel bleeding caused by lung cancer metastasis: Report of a case**  
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**Background**  
Small bowel bleeding due to malignancy is uncommon, of which carcinoid tumor is the most frequent cause. We herein describe a rare case of small bowel bleeding caused by metastatic tumor from lung cancer.

**Case**  
A 74-year-old man presented to our emergency department complaining of muscle weakness of the left side of the body. CT revealed a brain tumor in the right hemisphere and bilateral lung tumors. Because of progressive neurological deterioration, semi-emergency craniotomy with brain tumor resection was performed. Pathological examination of the specimen revealed poorly differentiated adenocarcinoma, which was suspected as metastatic tumor from lung cancer. A few days after surgery, he noticed graduate onset of hematochezia. Upper and lower gastrointestinal endoscopy were carried out, which failed to demonstrate abnormality. However, enhanced abdominal CT and MRI showed a tumor located in the small bowel. On 25 days after brain surgery, he developed massive melena, and transferred to our department where rapid fluid resuscitation was attempted, which failed to stabilize the hemodynamics condition of the patient. Therefore, emergency laparotomy was performed, in which intussusception of the ileum over an intra luminal solid tumor and mesenteric lymphadenopathy was identified. The lesion was resected. Histological examination confirmed poorly differentiated adenocarcinoma similar to that of the brain tumor. Despite multidisciplinary therapy, he died 3 months postoperatively due to progressive disease.

**Discussion**  
Metastatic small bowel tumor due to lung cancer is occasionally seen, but presentation as intussusception with massive bleeding as seen in this patient is rare.
P-10 Tumor budding detected by immunohistochemistry is not superior to hematoxylin eosin for predicting lymph node metastasis in pT1 colorectal cancer

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Background/Aims: Tumor budding in pT1 colorectal cancer has been reported as an important risk factor for lymph node metastasis. Detection of tumor budding by hematoxylin eosin staining is sometimes difficult due to desmoplastic reactions and it is easier by immunohistochemical staining. However, it still remains unclear whether immunohistochemical staining for the detection of tumor budding is useful for predicting lymph node metastasis in pT1 colorectal cancer. The purpose of this study was to clarify the clinical significance of tumor budding detected by immunohistochemical staining compared to hematoxylin eosin staining.

Methodology: Our study included 310 consecutive patients who underwent surgical resection of pT1 colorectal adenocarcinomas. Paraffin-embedded blocks showing the deepest tumor invasion were selected, and three 3-µm serial sections were re-cut from each block and assigned for hematoxylin eosin staining, anti-cytokeratin CAM5.2 staining, and a negative control. Tumor budding was defined as an isolated single cancer cell or a cluster of less than 5 cancer cells in the stroma in the invasive front area. One field in each section was selected for analysis.

Receiver operating characteristic curves were generated from the relationship between tumor budding counts and lymph node metastasis for hematoxylin eosin and CAM5.2 staining. The optimal cut-off values for each type of staining were determined from the receiver operating characteristic curves.

Results: Mean tumor budding counts detected by hematoxylin eosin and CAM5.2 staining were 3.5 ± 0.2 and 8.4 ± 0.5, respectively (p < 0.001). Receiver operating characteristic curve analyses revealed that the cut-off values for tumor budding detected by hematoxylin eosin and CAM5.2 staining for predicting lymph node metastases were 5 and 8, respectively. Moreover, the accuracy of tumor budding detected by hematoxylin eosin and CAM5.2 staining for predicting lymph node metastases was 73.2% and 59.7%, respectively.

Conclusions: Tumor budding counts detected by CAM5.2 staining were significantly higher than those detected by hematoxylin eosin staining. However, tumor budding detected by CAM5.2 staining was not superior to hematoxylin eosin staining for predicting lymph node metastases in pT1 colorectal cancer.
P-11 Evaluation of treatment for rectal neuroendocrine tumors of less than 20 mm in comparison with the WHO 2010 guidelines

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Background
Rectal neuroendocrine tumor (NET) is often difficult to evaluate an appropriate treatment for NETs of <20 mm in the clinical setting. Present guidelines and staging systems do not mention other clinicopathological variables. Although the WHO 2010 guidelines or TNM staging system do not mention the effect of lymphovascular invasion, this would be among the next promising targets for establishment of better guidelines and staging systems, particularly in early-stage colorectal NETs. We evaluated rectal NETs of <20 mm in comparison with the WHO 2010 guidelines.

Study Design
Between January 2005 and December 2013, 40 consecutive patients undergoing endoscopic resection of rectal NETs and 12 patients undergoing surgical resection of rectal NETs were enrolled in this retrospective study.

Results
There were 26 men and 14 women with a median age of 59.3 years. Median tumor size was 7.4 mm. Surgical procedures performed included rectal resection in 14 patients. Lymph node metastases were present in only 1 patient, whose tumors were 6-10 mm in size and who had lymphovascular invasion. NET recurrence was not detected in any patients. According to the WHO guidelines, tumors in 8 cases were classified as G1, 3 as G2, and 1 as G1/G2.

Conclusions
Histological examination of lymphovascular invasion is mandatory in specimens obtained by endoscopic resection, as this will provide useful information for determining the need for additional radical surgery with regional lymph node dissection. It is necessary to evaluate the treatment of NETs smaller than 20 mm as presently defined in the WHO 2010 guidelines.

P-12 Neoadjuvant treatment of lower rectal gastrointestinal stromal tumor (GIST) with imatinib successfully preserved anal function: A case report

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A 65-year-old woman underwent colonoscopy for fecal occult blood, which revealed a tumor, 31 mm in diameter in the left posterior wall of the lower rectum. Biopsy specimen was diagnosed as GIST (CD34 (+), c-kit (+)). MIB-1 positivity was within 10%, and the tumor was classified in low risk group. Because the tumor was located near the dentate line, anal preservation was judged difficult. She underwent imatinib treatment for 12 weeks (400 mg orally daily), and the tumor diameter reduced to 16 mm by MRI in 3 months, when transsacral rectal resection was performed which preserved anus. Although anastomotic leakage occurred, but controlled by conservative treatment.

Although the significance of neoadjuvant chemotherapy for GIST is not established, our case suggested the feasibility of neoadjuvant chemotherapy for low rectal GIST in order to facilitate anal preservation.
P-13  Colovesical fistula due to colonic diverticulitis in a young man: A case report

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We herein report a case with colovesical fistula due to colonic diverticulitis in a young man. A 37-year-old man was admitted to our hospital for painful urination and pneumaturia. Though he had been treated with levofloxacin at a primary hospital for a week, his condition did not improve. Enhanced computed tomography revealed chronic sigmoid diverticulitis with vesical adhesion and a few air bubbles in the bladder. Colonoscopy revealed chronic diverticulitis in the sigmoid colon and the scope could not be passed through the lesion because of stenosis. Cystoscopic examination revealed a vesical fistula. Barium enema examination demonstrated a few leakage of barium into the bladder. Taken together, a diagnosis of colovesical fistula due to colonic diverticulitis, the patient underwent partial colectomy and partial cystectomy with covering ileostomy. Histological examination revealed colonic diverticulitis and vesical inflammation. No malignancy was detected, and the diagnosis of colovesical fistula was confirmed. In the literature, colovesical fistula due to colonic diverticulitis is very rare in a young person.

P-14  Laparoscopic ileo-cecal resection: the total retro-mesenteric approach

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Ileo-cecal resection is the most performed procedure in Cohn's disease. In the last decades, the laparoscopic approach became the gold standard. The dissection can be lateral to median or median to lateral. In non-malignant diseases as it is the case for Crohn's disease, the most performed dissection approach is the lateral to median. Herein, we describe a technique performed in our department: the total retro-mesenteric approach.

METHOD:
The procedure requires 4 trocars with a 10- to 12-mm median suprapubic trocar. The telescope is placed in this trocar. The dissection will begin with the opening of the mesentery root creating a retro-mesenteric tunnel. This dissection gives a direct visualization of the duodenum, of the ureter and the gonadic vessels which guarantees a safe procedure considering the importance of the inflammation in this disease. At the end of the retro-mesenteric step, the right colon is only attached to the Toldt's fascia. The transection of the mesentery is done next to the bowel wall leaving at the end the choice to the surgeon to perform an extra- or endocorporeal anastomosis.

RESULTS:
This retro-mesenteric approach has been used in our department since 2004. Until May 2013, 89 patients underwent laparoscopic resection for Crohn's disease with a mean operative time of 130 min, a morbidity rate of 6 % and a laparoconversion rate of 13.6 %.

CONCLUSION:
We describe the total retro-mesenteric approach in the ileo-cecal resection for Crohn's disease. The approach is considered to be safe allowing the surgeon to perform a dissection far from the inflammatory site and allowing a visual identification of the duodenum and the right ureter. The morbidity of the procedure is equivalent to the other dissection techniques.
We report a case of Meckel's diverticulitis complicated by cystitis in an adult.

A 41-year-old man presented with lower abdominal and genital pain. He had a few similar episodes of lower abdominal pain over 2 years. Laboratory data showed a urinary tract infection (UTI) (Escherichia coli >10^6). Abdominal computed tomography revealed an intra-abdominal abscess above the urinary bladder. A Tc-99m pertechnetate scintigraphy was negative. Radiological enteroclysis showed a blind-end intestine, and retrograde urethrocystography failed to reveal a fistula between the intestine and urinary tract.

We diagnosed an abscess caused by Meckel's diverticulitis extending to the bladder and causing a UTI. We performed laparotomy to resect the Meckel's diverticulum, which was located 120 cm proximal to the ileocecal valve. Adhesions to the urinary bladder and sigmoid colon were present. The pathology of the Meckel's diverticulum showed ectopic pancreas tissue and abscess. Abdominal and genital pain resolved after surgery.

Meckel's diverticulum is the most common congenital condition of the gastrointestinal tract. Normally, a diverticulum is present in fetal life as the vitello-intestinal duct remnant, which usually disappears by the 7th week of gestation. It reportedly occurs in 1-3% of the general population and autopsy series. However, the lifetime risk of developing complications in patients with Meckel's diverticulum is believed to be less than 5%. Though most cases are difficult to diagnose and are found incidentally during surgery for another indication, we made the diagnosis preoperatively. In addition, Meckel's diverticulitis complicated by cystitis is rare. Accordingly, we report this case with some references.
P-17  Usefulness of abdominal ultrasonography for perforation of the small intestine caused by fish bone: A case report

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A 66-year-old woman was admitted to our hospital complaining of abrupt abdominal pain. Physical examination revealed symptoms of peritoneal signs in the mid-to-lower abdomen. She ate scorpion fish two days before admission, and mackerel a day before admission. Abdominal computed tomography demonstrated a high density line in the small intestine, accompanied by local peritonitis. Based on these findings, we entertained the diagnosis of peritonitis caused by an ingested fish bone. However, the exact location of the fish bone in relation to the intestine was not clear. By abdominal ultrasonography (US), the fish bone was judged to be penetrating the small intestine. Therefore we performed partial resection of the small bowel and removed the fish bone. Her postoperative course was uneventful.

P-18  Hepatocellular carcinoma with hemorrhagic infarction and central necrosis by auto-arterial embolism: Report of a case

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A 40-year-old male hepatitis B carrier visited our hospital for work-up and treatment of a hypoechoic lesion in the liver. Serum alpha-fetoprotein (AFP) was elevated to 37 ng/ml. Enhanced computer tomography (CT), and arteriography revealed a hypervascular tumor with a diameter of 25 mm in segment 5/6. However, preoperative CT after arteriography, revealed a high-density area in the tumor, which was suspected as hematoma. With a diagnosis of hepatocellular carcinoma (HCC) in the segment 5-6, the patient underwent extended-segmentectomy including the segment 6 and the dorsal half of the segment 5. Duration of the operation was 326 minutes, and intraoperative blood loss was 340 gram. Microscopic examination of the resected specimen revealed hemorrhagic infarction and central necrosis with arterial embolism in moderately differentiated HCC. The patient made a satisfactory recovery, and was discharged 9 days after resection. We herein reported a rare case of HCC with hemorrhagic infarction and central necrosis by auto-arterial embolism.
P-19  Serosal invasion strongly associated with recurrence after curative hepatic resection of hepatocellular carcinoma: A retrospective study of 214 consecutive cases

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Objective: The purpose of this study was to clarify the individual prognostic factors after curative and primary resection of hepatocellular carcinoma (HCC).

Methods: A retrospective search of our database identified 214 consecutive patients who underwent primary and curative hepatectomy for HCC at our department between January 1998 and December 2011. Risk factors for recurrence-free survival (RFS) and overall survival (OS) were analyzed with Cox proportional hazard model, Kaplan-Meier method, and log-rank tests.

Results: The 214 patients with HCC included 171 men (79.9%) and 43 women (20.1%). The median age of the patients was 65 years (range, 38-80 years). The distribution of pathologic Japanese stage was I: 19 (8.9%) cases, II: 115 (53.7%) cases, III: 55 (25.7%) cases, and IV (IVA): 24 (11.2%) cases. The median patient follow-up time was 49.5 months (range, 0.3-193.8 months). At the end of the follow-up period, 104 (48.6%) patients had died, and the median duration from the time of surgery to death in these cases was 34 months (range, 0.3 to 154.9 months). Tumor recurrence occurred in 140 (65.4%) patients, and the median time to recurrence was 17.4 months (range, 0.6 to 137.9 months). Significant correlations were identified between HCC recurrence and virus infection (HCV or others, P=0.0119), tumor size (≤2 or <2 cm, P=0.0135), formation of capsule (P=0.0123), and serosal invasion (P=0.0230). Multivariate analyses showed that serosal invasion (hazard ratio [HR], 2.75; P=0.0005) and vascular invasion (HR, 1.71; P=0.0331) were independently correlated with RFS. Tumor size (P=0.0193), vascular invasion (P=0.0131), and Japanese stage (P=0.0182) showed significant correlations with serosal invasion. The Kaplan-Meier method and log-rank tests revealed that the patients with serosal invasion showed significantly worse prognosis both in RFS (P<0.0001) and OS (P=0.0016). Among the 48 serosal invasion cases, 38 patients (79.2%) presented recurrence. The most dominant site of recurrence was the remnant liver, followed by the bone, lung, peritoneum, adrenal gland, lymph nodes, and pleura.

Conclusions: Serosal invasion should be regarded as one of the strong independent predictors for recurrence in curatively resected HCC cases. Such cases should be observed carefully and might require adjuvant therapy if it is applicable in the future.

P-20  NRAGE promotes the malignant phenotype of hepatocellular carcinoma

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Hepatocellular carcinoma (HCC) remains a deadly disease, mainly because effective therapy is limited to advanced or recurrent HCC. Therefore, it is critically important for improving outcomes to identify an informative biomarker for HCC progression as well as a molecular target for therapy. Neurotrophin receptor-interacting melanoma antigen-encoding protein (NRAGE), a member of the type II melanoma-associated antigen family, mediates apoptosis and cell death through interactions with diverse proteins and is implicated as a tumor suppressor or oncoprotein depending on cell type. However, the role of NRAGE in HCC is unknown. We used PCR and immunohistochemical techniques to determine the levels of NRAGE expression, as well as those of genes encoding potentially interacting proteins in HCC cell lines and in resected tumor and noncancerous liver tissues of 151 patients with HCC. The expression levels of NRAGE mRNA correlated significantly with those of apoptosis antagonizing transcription factor (AATF) and were not influenced by cirrhosis in noncancerous liver tissues, in contrast to elevated levels in HCC tissues. The expression patterns of NRAGE and its mRNA were consistent among 30 representative pairs of specimens. Increased NRAGE expression in HCCs correlated significantly with shorter disease-specific survival and was identified as an independent prognostic factors using multivariate analysis (hazard ratio 2.23, 95% confidence interval 1.06-3.83, P=0.020). Our results indicate that increased expression of NRAGE affects HCC progression via its interaction with AATF and may represent a novel biomarker and molecular target for therapy of HCC.
P-21 New strategy of cell transplantation: Hepatocyte transplantation using remnant organ with hepatocellular carcinoma after hepatectomy

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Recently large hepatectomy is very popular for hepatocellular carcinoma (HCC) and cholangiocarcinoma (CCC). However it is sometime happen that the patient who was performed large hepatectomy sometime became severe liver failure. This time, we paid attention to this resected liver, which contain a large amount of normal hepatocytes with carcinoma cell. In this study, we try to completely divide two group using FACS and transplant into syngeneic rats by using rat model.

We provide Immortalization rat hepatocytes that has SV40 largeT antigen as the artificial chromosome vector which we already developed in our laboratory. Those cells were used as cancer cell. At the same time, we marked those cells with GFP. And then, those cells were mixed with isolated hepatocytes, which were harvested from normal rats, and cultured them. As a next step, we made a division into two groups; normal and Immortals using FACS cell sorting by GFP marker.

We made complete separation into those two groups by GFP cell sorting method, but quality and quantity of separated normal hepatocytes were not enough to transplant.

So in this presentation, we report those result and conclusion in detail.

P-22 Clinical outcome of multidisciplinary treatment based on liver resections for multiple CRLM

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Background
It is very difficult to select the treatment for multiple CRLM. Recently, the therapeutic outcome based on surgical resections for multiple CRLM was improved dramatically, by the development of chemotherapy and molecular-targeted agents.

Patients and Methods
From April 2006 to August 2014, 36 patients with multiple CRLM underwent hepatectomy in our institute. We categorized the 36 patients into unilobular CRLM (group U; n = 20) and bilobular multiple CRLM (group B; n=16) according to the location of tumors. We retrospectively compared relevant clinicopathological variables, including patient and tumor characteristics and survival data, between these two groups.

Results
The mean age of study patients was 67.7 years (11 men and 5 women) and timings of liver metastases were synchronous in 14 cases, metachronous in 2 cases. The neoadjuvant chemotherapy (NAC) before liver resections were performed in 15 cases, they were repeated mean 10 courses (3-49). The mean number of tumors in group B was significantly larger than that in group U (group U: 3 vs group B: 8; p=0.002). The induction rate of NAC was also significantly higher in group B than group U (U 65% vs B 93.8%; p=0.04). The complication rate of group B was significantly higher than that of group U (U 10% vs B 56.3%; p=0.04). There were no significant differences between group U and B in both 3 year OS/DFS (OS: U 59% vs B 71.5%; DFS: U 11.8% vs B 15%, NS respectively). In group B, the early recurrence within 6 months after hepatectomy occurred in 7 cases (43.8%). These cases with the early recurrence had the significant poorer prognosis than other cases without the early recurrence.

Conclusions
There was no significant difference in the prognosis between unilobular and bilobular multiple CRLM patients by the development of multidisciplinary treatments. However the careful indication and strategy of liver resection is necessary for multiple CRLM, considering from the postoperative early recurrences.
P-23 Successful resection of a metastatic liver tumor from prostate cancer 14 years after radical prostatectomy; Report of a case

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A 70-year-old male who had undergone radical prostatectomy for prostate cancer 14 years previously visited our hospital for treatment of a liver tumor with a diameter of 54 mm. Serum PSA was elevated to 13.77 ng/ml. Abdominal computed tomography revealed a 54-mm solitary tumor in the segment 4. With the diagnosis of metastatic liver tumor from prostate cancer, the patient underwent medial segmentectomy. Microscopic findings of the resected specimen revealed a solid whitish tumor with hemorrhagic and necrotic changes in the central part, which was compatible with metastatic prostate cancer. The patient developed portal thrombosis on postoperative day 6, which was successfully treated by anticoagulation. Otherwise, the patient made a satisfactory recovery, and was discharged on postoperative day 15. We herein reported a extremely rare metastatic liver tumor from prostate cancer 14 years after radical prostatectomy.

P-24 Achievement of curative resection after chemotherapy with gemcitabine/cisplatin/S-1 for initially unresectable intrahepatic cholangiocellular carcinoma

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Biliary tract cancer including intrahepatic cholangiocarcinoma is not a rare disease and is one of the highly lethal malignancies. Although surgical resection is the only way to cure patients with biliary tract cancer, most patients are diagnosed at advanced stages. Chemotherapy is the major treatment for unresectable or post-operative recurrence biliary tract cancer. Combination chemotherapy of gemcitabine with cisplatin is the standard regimen with median overall survival and median progression-free survival of 11.7 and 8.0 months, respectively. However, this outcome is by no means satisfactory. We conducted combination chemotherapy of S-1, an oral fluoropyrimidine, with gemcitabine/cisplatin as a phase I study. Cisplatin (25 mg/m² i.v. for 120 min) followed by gemcitabine (1,000 mg/m² i.v. for 30 min) on day 1 and 8, and oral S-1 on alternate days; this regimen was repeated at 21-day intervals. A 57-year-old man with unresectable intrahepatic cholangiocarcinoma in the caudate lobe with paraaortic lymph node metastasis was enrolled in our study. No dose-limiting toxicities were observed during chemotherapy. As paraaortic lymph node metastasis was undetectable after 6 cycles of treatments, extended left hepatic lobectomy was performed on the patient. Pathological stage was stage IVB (pT2a, pN1, R0). The patient received adjuvant chemotherapy with S-1 for six months. At this point, he keeps cancer-free status. Phase II study was started based on the encouraging results from this phase I study.
P-25  Predictive factors of morbidity after surgical treatment of hepatic hydatid cyst

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Introduction Surgery remains the basic treatment of hepatic hydatid cyst (HHC). However, it is associated with significant morbidity. The aim of our study was to evaluate mortality and morbidity of surgery of the HHC and to highlight the risk factors.

Methods A retrospective study was conducted during 10 years. 391 patients hospitalized for HHC and operated in the Department of General Surgery “A” of the Rabta Hospital in Tunis, Tunisia.

Results The overall mortality rate was 0.7% while the overall morbidity rate was 20.4%. About 16.6% suffered from specific complications, while 3.8% suffered from non-specific complications. Predictors of morbidity in a univariate analysis included cysts larger than 9 cm, dome cysts, cysts with bilious contents, type II, III, IV or V on ultrasound classification, fissured cysts and intrabiliary rupture of hepatic hydatid cyst. The multivariate study consisted of independent predictors of disease at the site of the liver dome, the cysto-biliary fistula and intrabiliary rupture of hepatic hydatid cyst.

Conclusion The hepatic hydatid cyst of the dome and the existence of preoperative complications in particular intrabiliary rupture of hepatic hydatid cyst are the main factors of morbidity. A better understanding of these factors allows the surgeon to choose the appropriate surgical technique that is associated with less morbidity.

P-26  One case of chronic hydatid peritoneum

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Case: we present a well documented case of CHP. A male, 56 years old with abdominal pain, fever and an increasing in the volume of the abdomen is examined in the emergency room. The exam shows a diffuse abdominal tenderness. The number of white blood cells is elevated. The CT scann of the abdominopelvic area shows a huge abdominopelvic cyst which is difficult to relate to it’s origin. The liver is normal and ther is no ascites. Hydatid serlogy doesn’t realised because of the emergency context. Antibiotic therapy was started immediately and the patient was operated 2 days after admission. The diagnosis of CHP has been mentioned before laparotomy because of the high incidence of this pathology in North Africa. The image isn’t a typicall one and other diagnosis such mesenteric lymphangiomatous cyst is suspected to. At laparotomy, we discover a hyge cyst which measure 45 cm in diameter, mobile, with a soft consistency and seems to grow in the greater omentum. The cyst is attached to a small hydatid cyst developed in the lower surface of the segment V of the liver. The cyst was successfully removed in totality without incidence. Because, the cyst is attached to the lower side of the right liver. A cholecystectomy with a cholangiography were performed. There is no communication with intrahepatic bile ducts. The macroscopic exam shows a thick cyst wall with turbid liquid inside. There is no daughter vesicles. The patient recovers without any complications and was discharged at day 12. The definitive pathologic exam confirms the hydatid nature of the cyst.

Discussion: the opening of a hepatic hydatid cyst in the peritoneum occurs by two ways: acute form whith anaphylactic chock usually lethal and chronic form like our case. In CHP, the cyst is discovered later. The cyst migrates usually from a fissured liver hydatid cyst and grows in the peritoneum. The diagnosis is usually suspected in hydatic endemic area like Tunisia.

Conclusion: Chronic hydatidoperitoneum is a an exceptionnel presentation of hydatid cyst. It occurs by fissuration from a hydatid liver cyst.
Pre-emptive thoracic drainage to eradicate postoperative pulmonary complications after living donor liver transplantation

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Background: Thoracic fluid retention after living donor liver transplantation (LDLT) has various negative consequences, including atelectasis, pneumonia, and respiratory distress/failure.

Study design: We analyzed the clinical impact of preemptive thoracic drainage in 177 patients undergoing adult-to-adult LDLT for chronic liver diseases at a single center. Recipients were divided into two time periods. Earlier cohort (n=120) was analyzed for risk factors for postoperative atelectasis retrospectively, whereas later cohort (n=57) with a risk factor for postoperative atelectasis underwent preemptive thoracic drainage prospectively. The incidence of postoperative pulmonary complications was compared between these two cohorts.

Results: Independent risk factors for atelectasis in earlier cohort were body mass index ≥27 kg/m² (p < 0.001), performance status ≥3 (p = 0.003) and model for end-stage liver disease score ≥23 (p = 0.005). The rates of atelectasis (21.1 vs 42.5%, p = 0.005) and pneumonia (1.8 vs 10.0%, p = 0.049) were significantly lower in later than in earlier cohort. Moreover, the mean durations of intensive care unit stay (3.6 ± 0.2 vs 5.7 ± 0.6 days, p = 0.038) and postoperative oxygen support (5.1 ± 0.8 vs 7.1 ± 0.5 days, p = 0.037) were significantly shorter in later than in earlier cohort. There were no significant differences in the incidence of adverse events associated with thoracic drainages between these two cohorts.

Conclusions: Preemptive thoracic drainage for transplant recipients at high risk of postoperative atelectasis could decrease morbidities after LDLT.

Utility of augmented reality system in hepatic surgery

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Background and Objective: Since 2006, we have been developing a navigation system using augmented reality (AR) technology and have reported clinical application for hepatobiliary pancreatic surgery under laparotomy. This superimposed system in the hepatic surgery can be expected to contribute to surgery accuracy and efficiency. We here report the results of hepatic surgery using AR technology and problems found during the surgery.

Method: Seven patients were operated on this system. The breakdown of the patients are as follows; 3 had metastatic liver carcinoma and 4 had hepatocellular carcinoma (2 with laparoscopic surgery). We created a reconstructed model by preoperative multi-detector computed tomography. Registration between visceral organs and the reconstructed surface-rendering image was carried out with an optical location sensor. We filmed the operative field with a short rigid stereo-scope and showed the reconstructed model and the image on stereoscopic display monitor. 3D glasses were used during the procedure. We examined the position of the registration, the average error, the visibility and the usefulness.

Results: Because registration was performed by soft tissues such as the liver edge and the falciform ligament in addition to vessel bifurcations, the error was greater than in cases with registration in the vascular structures alone (6.6mm : 8.9mm ). We calculated its average accuracy by fiducial registration error. 3D visibility of the monitor was good and we were able to obtain information on deep parts of the body. On usefulness, the average error was larger compared to pancreaticoduodenectomy that was carried out by registration of vessel bifurcation alone. This was attributed to deforming from postural change and limited registration points. Repeated registration during dissecting of the liver improved accuracy and we were able to easily identify the Glisson’s sheath and the hepatic vein after words.

Conclusion: Although the hepatic navigation surgery under laparotomy has room to improve in registration method and in corresponding to deformity, our efforts suggests that repeated registration during dissecting the liver increases accuracy.
Feasibility of laparoscopic liver resection for liver tumors in high-risk patients

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Introduction: Laparoscopic liver resection (LLR) has been widely spreading as a new option of surgery for liver disease. The aim of this retrospective study is to examine the feasibility and safety of LLR in high-risk patients.

Methods: Favorable indications of LLR are partial resection or left lateral sectionectomy for tumor located in left-lateral segment or inferior segments (S4b, S5, and S6). With the accumulation of our experience, major LLR has been introduced for tumors beyond these indications. Patients who have been pre-operatively evaluated to have insufficient organ functions other than liver, including chronic cardiac disease above NYHA class II, chronic obstructive pulmonary disease above stage III, chronic kidney disease above stage III, Insulin dependent diabetes mellitus, cerebral vascular accident with residual neurological deficit, were classified into the “high-risk” group. Peri-operative data of LLR in high-risk patients were compared to the common-risk patients. Comparison of quantitative variables was performed using the Chi-square test. The t test was used to compare continuous variables.

Results: Out of 202 LLRs, 69 patients including 6 major hepatectomies were classified into high-risk group with a mean age of 66.9. There were no significantly differences between the high-risk and the common risk groups in operative blood loss (285.4cc vs. 309.6cc), operative duration (290.7min. vs. 313.6min.), post-operative hospital stay (11.0days vs. 10.4days) and morbidity (13.0% vs. 11.3%). No carbon-dioxide gas embolism, post-operative liver failure or mortality was found in both groups.

Conclusion: With stringent patient selection and peri-operative management, LLR can be safely performed and is feasible in high risk patients.

Curative resection after gemcitabine, cisplatin and S-1 chemotherapy for initially unresectable biliary duct cancer:

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A 68-year-old woman was diagnosed with unresectable upper bile duct cancer with suspected invasion of the right hepatic artery and para-aortic lymph node metastasis (T4N3M0, Stage IVb). She underwent plastic stent placement for obstructive jaundice and enrolled in our phase I study for unresectable biliary tract cancer consisting of cisplatin (25 mg/m² i.v. for 120 min) followed by gemcitabine (1,000 mg/m² i.v. for 30 min) on days 1 and 8, and oral S-1 on alternate days. After 8 courses of the neoadjuvant chemotherapy without adverse effect, computed tomography showed near-complete disappearance of the tumor of the upper bile duct and swollen lymph nodes. She then underwent subtotal stomach-preserving pancreaticoduodenectomy and lymph node dissection. The pathological stage was pT1N0M0, Stage I. The patient made a satisfactory recovery, was discharged on 29 days after operation, and remains free of disease under adjuvant chemotherapy using S-1 as of 3 months after the operation.
P-31 Non-specific inflammatory sclerosing cholangitis mimicking lower bile duct cancer : A case report

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A 30-year-old male visited our hospital for work-up and treatment of obstructive jaundice. Abdominal enhanced computed tomography (CT) revealed wall thickening and a tumor with enhancement in the lower bile duct. Magnetic resonance imaging (MRI) showed a low-intensity area around the lower bile duct on T1-weighted images. Endoscopic retrograde cholangiopancreatography (ERCP) revealed stenosis in the lower bile duct, and endoscopic ultrasonography (EUS) showed sonazoid-enhancement of the hyperechoic stricture. Brush cytology during ERCP was diagnosed as class III. The laboratory investigation included serum total bilirubin of 6.7 mg/dl, CEA of 1.2 ng/ml, CA19-9 of 25 U/ml, elastase 1 of 430 ng/dl, DUPAN-2 of 48 IU/l, and serum IgG4 of 48 U/ml. Because of young age of the patient, and the possibility of lower bile duct cancer, the patient underwent pancreaticoduodenectomy. Duration of operation was 436 minutes, and intraoperative blood loss was 430 gram. Macroscopic finding of the resected specimen revealed a stenotic lesion with wall thickening in the lower bile duct. Microscopic findings indicated lymphoplasmic inflammatory infiltration and fibrosis under the lower bile duct mucosa without malignancy or IgG4 positive. The patient made a satisfactory recovery, and was discharged on postoperative day 15. We herein reported a resected case of non-specific inflammatory sclerosing cholangitis mimicking the lower bile duct cancer.

P-32 Surgical outcomes in patients with gallbladder carcinoma diagnosed after cholecystectomy

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【Background】Diagnosis of gallbladder carcinoma is difficult due to the lack of reliable diagnostic methods and specific clinical features. Particularly in case of early cancer or of accompanying inflammation.

【Objective】To explore surgical strategies for gallbladder carcinoma diagnosed after cholecystectomy.

【Methods】Between 1990 to 2014, 100 patients who underwent resection for gallbladder carcinoma were studied. Pathological diagnosis was as follows. Suffix p indicates pathologically confirmed, T1 is the involvement of the mucosal layer or the muscularis propria, T2 means invasion of the perimuscular connective tissue but no extension beyond the serosa or into the liver, and T3 means invasion of the serosa.

【Results】Sixteen patients were diagnosed as gallbladder carcinoma after cholecystectomy by histological examination of resected specimen. Median age was 64 (47-81) years. Eight patients were male, and 8 patients were female. Nine patients were transferred after initial cholecystectomy at other hospitals. Fourteen patients underwent laparoscopic cholecystectomy, and 2 patients underwent open surgery. The numbers of pT1, pT2 and pT3 patients were 5, 6 and 5, respectively.

In pT1 group, 4 patients were followed up without additional treatment after initial surgery. One patient underwent extrabiliary bile duct resection due to pathological residual tumor of cystic duct. During the follow-up period (median 84 months), all patients are alive with no tumor recurrence except one death of other disease. In pT2 group, 4 of 11 patients had residual tumor tissue. Reoperation, included regional lymph node dissection, partial hepatectomy of the gallbladder bed and extrabiliary bile duct resection, was performed, and then R0 resection was achieved in all cases. Lymph nodes metastases were observed in 4 patients (36%). Five-year survival rates were 83% in pT2 group and 50% in pT3 group, respectively. Tumor recurrence was observed in 3 patients (lung 1, liver 1, local recurrence 1). Post site recurrence was not observed in patients after initial laparoscopic cholecystectomy.

【Conclusions】In pT1 group, as favorable prognosis was achieved with cholecystectomy alone, there would be no need for reoperation in patients with early cancer without pathological cancer residual. In pT2 and pT3 group, reoperation included lymph nodes dissection and extent resection with curative intent would contribute better prognosis.
P-33 Needle-knife sphincterotomy vs. guidewire-assisted transpancreatic sphincterotomy for difficult biliary cannulation

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AIM:
Needle-knife sphincterotomy (NKS) is a commonly used precut technique for difficult biliary cannulation. Guidewire-assisted transpancreatic sphincterotomy (GATS), as an alternative method for bile duct entry when conventional biliary cannulation failed, has been debated on its success rate of cannulation and its complications, such as increased incidence of pancreatitis. This study was aimed to compare success rate, and complications of NKS and GATS for difficult biliary cannulation.

METHODS:
This was a retrospective study conducted between April 2006 and November 2014 in a single university hospital in Japan. We defined difficult cannulation as biliary cannulation failure by conventional, wire-guided and pancreatic guidewire technique. A total of 32 difficult cannulation patients, were divided into NKS (n = 10) and GATS (n = 22) groups. NKS or GATS was done for selective biliary cannulation. We measured the technical success rates of biliary cannulation and procedure related complications.

RESULTS:
Both groups were comparable in baseline characteristics. Successful cannulation rate in NKS and GATS groups were 90.0% vs. 90.9%, P = 0.732, respectively. There was no significant difference between both groups. The overall incidence of post-endoscopic retrograde cholangiopancreatography (ERCP) pancreatitis was 20.0% vs. 13.6%, P= 0.0211 in NKS and GATS group; post-procedure pancreatitis was significantly higher in NKS group. The overall incidence of post-ERCP hyperamylasemia was no significant difference between both groups; NKS vs. GATS group: 40.0% vs. 36.4%, P=0.235. Pancreatic stent was inserted to prevent post-ERCP pancreatitis 60.0% vs. 100%, P= 0.0142 in NKS and GATS group.

CONCLUSION:
In difficult cannulation cases, NKS and GATS facilitated biliary cannulation and showed similar success rates. However, post-procedure pancreatitis was significantly higher in NKS group. Pancreatic stent insertion may be needed to prevent post-ERCP pancreatitis in NKS.

P-34 The evaluation of chemo-radiation therapy for the borderline resectable pancreatic cancer

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Introduction: Based on the results which chemotherapy of S-1 single use combined with radiation (chemo-radiation therapy; CRT-01) was safety and effective for advanced pancreas cancer, the additional trial with Gemcitabine (CRT-02) has been studied.

Patients and Methods: Of the patients with borderline resectable pancreas cancer clarified by NCCN guide line, CRT-01 (80mg/m2/day of S-1 with 39.6Gy radiation) for twelve patients from Sep/2009 to Jan/2013 and CRT-02 (addition of 1000mg/m2 Gemcitabine with CRT-01) for eight patients from Feb/2013 were performed. The operation was planned between four and ten weeks after treatment. To evaluate the significance of present CRT, the prognostic outcomes were compared to thirty-seven cases of advanced pancreas cancer (twenty resected and seventeen un-resected) without preoperative therapy (NCRT).

Result:
1. On the patients (male female ratio=11: 9 and average age was 64.5 y.o., range; 49-81) with 32 days treatment term, range; 29-49 days, adverse events with grade3 or more adverse events were just detected for four cholangitis and three neutropilia. Except resected eight cases by pancreatoduodenectomy and two by distal pancreatectomy, serious artery invasion and newly appearance of distant metastases were found for six and two respectively. 2. In the resected cases with ten CRT cases and twenty NCRT cases, the duration of operation (min) was 390±101 and 379±56 and total blood loss (ml) was 922.5±708.4 and 778.5±430.4. 3. The rate of post-operative complications were detected for 25% pancreas fistula, 25% delayed gastric empty and 10% ischies in NCRT, but for just 12.5% pancreas fistula in CRT. 4. The disease free survival (DFS; days) was calculated for 252±51 and 547±307 with resected cases of NCRT and CRT. 5. In the un-resected cases, the DFS of ten CRT cases, 618 = 162, was significantly longer than seventeen NCRT cases, 186 ± 50, but, median survival term was almost similar (647 = 57 vs. 578 = 222).

Conclusion: The CRT was performed safety, and the prognostic effect might be expected even for quite advanced pancreas cancer.
P-35 Association of tumor budding with clinicopathological characteristics and prognosis in pancreatic ductal adenocarcinoma

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[Background/Aims] Pancreatic ductal adenocarcinoma (PDAC) is one of the most aggressive and lethal human malignancies. Classical histomorphological features like tumor size, tumor grade, blood vessel or lymphatic invasion, presence of lymph node metastases and margin status constitute essential prognostic determinants in PDAC. Tumor budding, defined as the presence of de-differentiated single tumor cells or small cell cluster at the invasive front of carcinoma such as colorectal and oesophageal, is a prognostic factor. The aim of this study was to assess the prognostic impact of the tumor budding in PDAC.

[Methodology] A total of 81 resected cases of PDAC was examined. All of the resected specimens were cut stepwise at 4 mm interval, and all of the blocks were paraffin-embedded. After selecting a block in which tumor size was maximal, three serial 3-µm-thick sections were prepared from each block. We defined tumor budding as an isolated single cancer or a cluster composed of fewer than five cancer cells. Whole-tissue sections were stained using a hematoxylin-eosin (HE) staining or a pancytokeratin marker (AE1/AE3). Tumor budding was assessed in a microscopic field of x200 and counted. Cutoff points of the budding were determined using χ² scores calculated with the Cox proportional hazards regression model. Furthermore, the selected sections was stained using a pancytokeratin marker (AE1/AE3) and MIB-1 monoclonal antibody that have been used as markers of proliferative potency. We defined budding cancer cells with immunoreactivity of MIB-1 have proliferative potency.

[Results] Cutoff points of the budding was 13 or more (χ² = 9.236, P = 0.002) in HE stained sections and 15 or more (χ² = 9.236, P = 0.002) in sections with AE1/AE3 immunohistochemistry. High grade budding evaluated with both standard HE (11.1% cases) and AE1/AE3 staining (43.2% cases) correlated significantly with poor overall survival and the histological grade. The cumulative 2-year survival rates were 43.1% for patients with low grade budding and 0% for patients with high grade budding stained with standard HE (P < 0.001). Multivariate analysis revealed that the margin status, lymph node metastasis, the high grade budding assessed by HE staining and the high grade budding with proliferative potency assessed by AE1/AE3 and MIB-1 double immunostaining were independent prognostic factors.

[Conclusion] The high grade budding is a strong and independent prognostic factor. Tumor budding counts detected by AE1/AE3 staining were significantly higher than those detected by HE staining. Tumor budding, however, detected by AE1/AE3 immunostaining was not superior to HE staining for predicting survival in PDAC.

P-36 Effectiveness of plasma treatment on pancreatic cancer cells


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Backgrounds. Plasma is referred to as “the fourth state of matter” that is subsequent to solid, liquid and gas, and resides in a high-energy state composed of negative electrons, positive ions, free radicals, excited molecules and energetic photons. Conventionally, plasma has been generated under high temperature and low pressure; however, owing to technical developments, non-equilibrium atmospheric pressure plasma (NEAPP), also known as cold plasma or non-thermal plasma, has actually entered into the realm of practical use. Recently, NEAPP therapy has attracted attention as “the fourth cancer therapy”, which is subsequent to surgery, chemotherapy and radiotherapy. The antitumor effects of plasma have been reported in various cancer cell lines, and were thought to be associated with generation of reactive oxygen species (ROS), leading to DNA damage, cell cycle arrest and finally induction of apoptosis. Some previous studies reported the direct effects of plasma treatment on the cells. In recent years, it has been reported that glioblastoma brain tumor cells and ovarian and gastric cancer cells could be selectively induced to undergo apoptosis when treated with plasma-activated medium (PAM).

Objectives. We explored the indirect effect of NEAPP through plasma-activated medium (PAM) on pancreatic cancer cells in vitro and in vivo.

Methods. Four pancreatic cancer cell lines were used and the antitumor effects of PAM treatment were evaluated using a cell proliferation assay. To explore functional mechanisms, morphological change and caspase-3/7 activation in cells were also assessed. Furthermore, reactive oxygen species (ROS) generation in cells was examined and N-acetyl cysteine (NAC), an intracellular ROS scavenger, was tested. Finally, the antitumor effect of local injection of PAM was investigated in a mouse xenograft model.

Results. The cell proliferation assay showed that PAM treatment had lethal effect on pancreatic cancer cells. Typical morphological findings suggestive of apoptosis such as vacuolization of cell membranes, small and round cells and aggregation of cell nuclei, were observed in the PAM treated cells. Caspase-3/7 activation was detected in accordance with the observed morphological changes. Additionally, ROS uptake was observed in all cell lines tested, while the antitumor effects of PAM were completely inhibited with NAC. In the mouse xenograft model, the calculated tumor volume on day 28 in the PAM-treated group was significantly smaller compared with the control group (28 = 2.2 vs. 89 ± 38 (mm³ ± SD), p=0.0031). Histological analysis of tumors from each group showed that approximately 60% of tumor cells were degenerated in the PAM-treated group.

Conclusions. PAM treatment showed antitumor effects on pancreatic cancer cells, which induced apoptosis through intracellular ROS generation. PAM treatment of pancreatic cancer might be a promising therapeutic strategy.
**P-37** Inhibition of nuclear factor Kappa-B enhances the antitumor effect of combination treatment with gemcitabine and Nab-Paclitaxel for pancreatic cancer cells

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**Introduction.** Nuclear factor-κB (NF-κB) plays an important role in promoting growth, angiogenesis, and metastasis in pancreatic cancer, and serves as a mechanism underlying therapeutic resistance. Pomalidomide is an investigational immunomodulating drug (IMiDs) of thalidomide under development that also inhibits angiogenesis and induces apoptosis. We hypothesized that pomalidomide inhibits the anticancer agent-induced NF-κB activity and enhances the antitumor effect of combination treatment with gemcitabine and nab-Paclitaxel for pancreatic cancer.

**Methods.** We assessed NF-κB activity and cell viability of a human pancreatic cancer cell line (MIA PaCa 2, PANC 1) treated with gemcitabine alone, both gemcitabine and nab-Paclitaxel, triple combination of gemcitabine, nab-Paclitaxel, and pomalidomide, or vehicle as control. NF-κB activation was evaluated by measuring nuclear localization of p65 protein.

**Results.** NF-κB activity of anticancer agent groups were higher than that in control group (p<0.01). Pomalidomide significantly inhibited anticancer agent-induced NF-κB activity (p<0.01). Cell apoptosis was the highest in the triple combination group compared with that in combination of gemcitabine and nab-Paclitaxel in MIA PaCa 2 (p<0.05). Cell viability in triple combination group was lower than that in gemcitabine alone, or combination of gemcitabine and nab-Paclitaxel groups in MIA PaCa 2 (p<0.05, respectively).

**Conclusions.** Inhibition of NF-κB by pomalidomide enhances the antitumor effect of combined gemcitabine and nab-Paclitaxel for pancreatic cancer cells.

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**P-38** Laparoscopic fenestration for a symptomatic huge splenic cyst with Gaucher’s disease: Report of a case

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A 34-year-old woman visited our hospital for treatment of a huge splenic cyst with epigastric pain. The patient was diagnosed as Gaucher’s disease (type 1) at 3 years of age, and has been receiving enzyme replacement therapy (ERT) from 15 years of age. Abdominal MRI revealed a low-intensity area 30 cm in diameter with well-defined borders on T1-weighted images. Because epigastric pain due to the huge splenic cyst worsened, the patients underwent laparoscopic splenic cyst fenestration. The huge splenic cyst contained 2,500 ml of brownish-red fluid. The patient made a satisfactory recovery, and was discharged on the postoperative day 11. Gaucher’s disease is an extremely rare metabolic disease: approximately 5,000 patients in the world, and 100 patients in Japan. We herein reported an extremely rare case of a symptom huge splenic cyst with Gaucher’s disease treated by laparoscopic fenestration.
**P-39**  
**ZEB-1 and E-cadherin expression may predict recurrence-free survival in patients with invasive ductal breast carcinoma**

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Background: Epithelial-Mesenchymal Transition (EMT) plays an important role in cancer progression and metastasis. We investigated the expression of two EMT-related molecules, ZEB-1 and E-cadherin, in invasive ductal breast carcinoma and evaluated their association with clinicopathological parameters and recurrence-free survival.

Methods: We evaluated the expression of ZEB-1 and E-cadherin in 116 patients of Stage I, II, and III primary invasive ductal breast carcinoma (mean age, 58.5 years, male: female = 0:116) using immunohistochemistry. ZEB-1 expression was immunohistochemically categorized as positive if over 5% of stromal fusiform cells around the epithelial cancer cells show nuclear staining. E-cadherin expression was regarded as reduced if whole tumor cells were stained weak, or peripheral part such as tumor infiltration to fatty tissue were stained less than central part of tumors.

Results: Of the 116 patients, 51 (44%) had Stage I, 58 (50%) had Stage II, and 7 (6%) had Stage III tumors. Thirty seven patients (32%) had lymph node metastasis. One hundred and one patients (87%) had ER positive tumors, and 20 patients (17%) had HER2 positive tumors. Positive ZEB-1 expression was observed in the tumors of 66 patients (57%), but it was not significantly associated with clinicopathological parameters. Reduced E-cadherin expression was observed in the tumors of 34 patients (29%). It was significantly associated with negative estrogen receptor expression. Patients with a positive ZEB-1 and / or reduced E-cadherin had a poorer outcome than the other patients in terms of recurrence-free survival.

Conclusion: ZEB-1 and E-cadherin expression may predict recurrence-free survival in patients with invasive ductal breast carcinoma.

Keywords: Breast carcinoma, ZEB-1, E-cadherin, EMT

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**P-40**  
**Palliative treatment with self-expandable metallic stent (SEMS) for colorectal malignant obstruction**

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INTRODUCTION:  
Transanal ileus tube or emergency surgery is often indicated as a treatment for colorectal malignant obstruction. The treatment with SEMS was accepted by Japan medical insurance in 2012. After approval for insurance coverage, SEMS placement is getting popular as a treatment for obstructing colorectal malignancy. SEMS placement is expected to be an effective treatment for the purpose of avoiding emergency surgery.

However, the safety and usefulness of treatment with SEMS for colorectal malignant obstruction are controversial.

AIM:  
To clarify the safety and usefulness of SEMS for palliation of colorectal malignant obstruction.

PATIENTS AND METHODS:  
From April 2014 to February 2015, eight patients were treated for colorectal malignant obstruction with SEMS. There were four males in the present study, and the mean age of them was 83 years. Seven patients were diagnosed as colorectal malignant obstruction due to colonic cancer, and one as malignant obstruction due to pancreatic cancer. In the present study we investigated the safety and usefulness of SEMS as treatment for obstructing colorectal malignancy.

RESULTS:  
For six patients, SEMSs were placed successfully, and they could have a meal again after colonic obstruction was improved. In one of six patients, migration of SEMS was observed as late complication during chemotherapy. Surgical intervention was performed for two patients. In one case, the guidewire couldn’t pass through malignant obstruction, while in another case, a stent was mislocated to an appendix.

CONCLUSIONS:  
For palliative treatment of malignancy-induced colorectal obstruction, SEMS is an efficient and safe tool associated with minimal intervention, and also SEMS can relieve physical and mental stress, and improve their Quality of life.