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## Development of endoscopic surgery for the minimally invasive treatment of digestive and other diseases

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**Abstract.** Minimally invasive surgery has rapidly changed the performance of surgical practice in a wide range of surgical specialities in the last decade of the 20th century. The marked progress in endoscopic surgery has been conducted especially in general and digestive surgery. The Department of Surgery, School of Medicine, Keio University has contributed to the development and establishment of endoscopic surgery in every subspeciality of general and digestive surgery. Our achievements include the development of original methods for laparoscopic wedge gastrectomy and endoscopic thyroidectomy, establishment of surgical techniques in endoscopic surgery for esophageal, gastric, colorectal and hepatobiliary diseases, and the introduction of robotics and tele-communicative technologies to endoscopic surgery. (Keio J Med 50 (3): 167–174, September 2001)

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The pain, discomfort, and disability, or other morbidity occurring as a result of surgery are more frequently due to trauma involved in gaining access to the area to perform the intended procedure rather than from the procedure itself. For example, following a cholecystectomy, the need for hospitalization is not related to the removal of the gallbladder but rather is necessary because of pain from the trauma to the abdominal wall caused by the incision to gain access to the gallbladder.<sup>1</sup> In comparison with open surgery, laparoscopic surgery results in less postoperative pain, shorter hospitalization, more rapid return to the work force, a better cosmetic result, and a lower incidence of postoperative intra-abdominal adhesions. Following the introduction of laparoscopic cholecystectomy by Mouret in France, the use of the minimally invasive approach has rapidly changed the performance of surgical procedures in a wide range of surgical specialities, including general surgery, urology, gynecology, thoracic surgery, plastic surgery, and cardiac surgery.

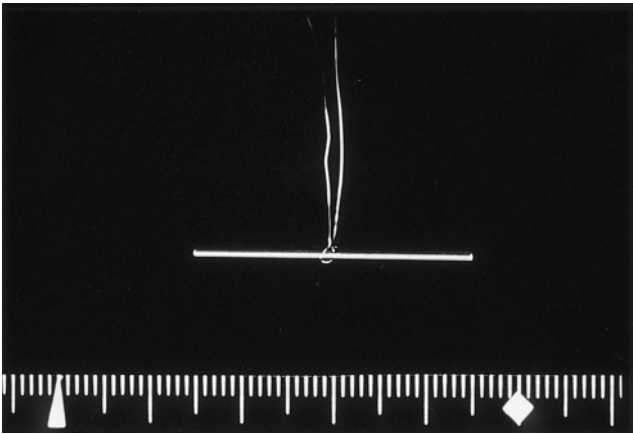
The Department of Surgery, School of Medicine, Keio University first performed laparoscopic surgery in 1990, shortly after the primary success was reported in the United States, and since that time, has continued the development and establishment of laparoscopic surgery as one of the most advanced institutes worldwide.

### Development of Laparoscopic Surgery for Gastric Diseases

#### *Laparoscopic wedge gastrectomy for early gastric cancer*

The most typical achievement of our department was the development of laparoscopic procedures for the treatment of early gastric cancer.

Asymptomatic early gastric cancer, especially lesions in which infiltration is limited to the mucosa, have been frequently detected through a well-established screening program in Japan. The accuracy of the preoperative diagnosis of the depth of cancerous infiltration for



**Fig. 1a** A device to lift lesions termed the 'lesion-lifting set'; a 2–3 cm metal rod with a fine wire at the center is introduced through the outer sheath into the stomach.



**Fig. 1b** The lesion is accurately lifted using the metal rod by pulling the wire.

mucosal gastric cancer is as high as 90% by endoscopy and endoscopic ultrasonography. Therefore, it is important to establish a minimally invasive therapy for mucosal gastric cancer. Among 483 consecutive patients with mucosal gastric cancers who underwent gastrectomy with lymph node dissection in our institution, lymph node metastasis was found in only 10 (2.1%), most of whom had large, depressed lesions with ulcers or scar formation. There was no lymph node metastasis when the diameter of the lesion was less than 25 mm. Most mucosal gastric cancers can thus be curatively treated by local resection of stomach tissue. To obtain both a complete cure and minimal invasiveness, we introduced an original laparoscopic treatment for early gastric cancer since 1992.<sup>2</sup> The technique was termed the lesion-lifting method.

After laparoscopic exposure of the gastric wall around a cancerous lesion, a small metal rod is introduced into the stomach at the vicinity of the lesion through a catheter which pierces the abdominal wall and the exposed gastric wall. While the cancerous lesion is accurately lifted up with the support of the metal rod (Figs. 1a & 1b), wedge resection of the stomach is carried out using an endoscopic stapling device. This procedure results in complete local resection of the lesion with a sufficient surgical margin.<sup>3,4</sup>

We have successfully treated 111 patients with early gastric cancer using the laparoscopic approach. There have been two recurrences, both of which were mucosal lesions found 2 years after the initial surgery, and were successfully treated with gastrectomy and laser irrigation. All patients survived for 3 to 96 months. To date, our method has been recognized as a curative and minimally invasive treatment for early gastric cancer, and are applied worldwide.

#### *Application to gastric submucosal tumors*

Asymptomatic gastric tumors are frequently detected through screening programs, and include submucosal tumors as well as early gastric cancers. Unfortunately, it is often impossible to evaluate the malignant potential of the tumors based on the results of endoscopic biopsy, endoscopic ultrasonography, or computed tomography. Even with EUS-guided aspiration biopsy, the tissue specimens are usually too small to make a pathologic diagnosis. As it has been indicated that small leiomyosarcomas possess malignant potential, patients with a gastric SMT are treated by open surgery. However, the treatment of malignant stromal tumors including leiomyosarcomas is controversial. Of the 28 patients with leiomyosarcoma who underwent open surgery between 1984 and 1994 at our institute, no lymph node metastases were detected at the time of operation.<sup>5</sup> Furthermore, there were no difference in survival between systemic lymph node dissection and nondissection groups. Conversely, tumor size and histologic grade can be used to predict disease-free survival after curative resection. Therefore, to make a pathologic diagnosis and to ensure the removal of the lesion, wedge resection for small leiomyosarcomas is the first line treatment of a gastric SMT. Thus, laparoscopic wedge resection of the stomach, first introduced for the treatment of early gastric cancer at our institute, has also been applied to the treatment of SMTs of the stomach since 1993.<sup>6</sup>

Over 50 patients with SMTs of the stomach underwent laparoscopic wedge gastrectomy. The tumors ranged from 8 to 60 mm in diameter. All surgical margins were clear. The average operative time was 131 minutes. Conversion to open surgery was needed in

only one patient with a tumor along the lesser curvature of the mid-portion of the stomach because of obesity. Most of the patients began eating on the first operative day and were discharged within 5 to 7 days. Histopathological examination of the tumors showed gastrointestinal stromal tumor, ectopic pancreas, leiomyosarcoma, schwannoma, carcinoid, leiomyoma, an inflammatory lesion caused by parasites, and cysts. No recurrences were observed over the 5-year follow-up period. It is suggested that laparoscopic wedge resection of the stomach for an SMT is a safe, curative, and minimally invasive procedure, if the patients are carefully selected.

#### *Application of sentinel node navigation surgery to laparoscopic gastrectomy*

Curative resection for invasive gastric cancer should include removal of the lymphatic drainage of the tumor-bearing segment of the stomach. Gastrectomy with systematic lymph node dissection (D1 or D2) has been considered as a standard procedure for the treatment of early gastric cancer with potential for micro-lymph node metastases. The frequency of lymph node involvement, however, is less than 15% in early gastric cancer, in which the depth of invasion is limited within the submucosal layer.<sup>7</sup> Simple wedge resection with a safe surgical margin should be sufficient for curative treatment for early gastric cancer without lymph node metastases. From this point of view, distal or total gastrectomy with lymphadenectomy, for patients with early gastric cancer without lymph node metastases, might be regarded as an excessive surgery. The difficulty in the preoperative diagnosis of the micro-lymph node involvement, however, is the reason why conventional gastrectomy with lymphadenectomy remains valid as a standard procedure.

The sentinel node concept is based upon the orderly progression of tumor cells within the lymphatic system. The first draining node, called the sentinel node, is also the first to contain metastases. Identifying the sentinel node can be accompanied by preoperative injection of radioactive isotope-labeled colloidal albumin at the site of the primary tumor and subsequent intraoperative use of a handheld gamma probe to localize radioactivity in the lymph lesion. The technique can also be performed with a vital blue dye which enables visualization of the lymphatics. Sentinel node biopsy has been performed in patients with melanoma and those with breast cancer, and the histological status of the sentinel node accurately predicted the lymph node status.

We introduced this technique to gastrointestinal cancers to assess the extent of lymphadenectomy in each patient since 1999.<sup>8</sup> In a pilot study in open surgery, both of the detectable and predictive rates of

sentinel nodes in patients with gastric cancer were higher than 95%. Using this technique, our curative laparoscopic procedure, which was originally developed for the minimally invasive treatment of mucosal cancers, may be applicable to patients without lymph node metastases confirmed by intraoperative sentinel node biopsy. We confirmed the feasibility of laparoscopic detection of sentinel nodes in early gastric cancer, using the abdominal gamma probe in a preliminary study. There are several issues to resolve for a clinical trial of laparoscopic sentinel node navigation surgery of early gastric cancer, such as the laparoscopic technique for radio-guided sentinel node detection, and the sensitivity of intraoperative pathologic examination of micro-metastases in the sentinel nodes. However, we note that it is worthwhile to continue evaluating this technique to determine its role in a minimally invasive approach to early gastric cancer.

#### **Development of Endoscopic Surgery for Thyroid Diseases**

Postoperative cosmesis in the neck is often a major concern of patients, particularly those undergoing thyroid surgery. Therefore, the performance of thyroidectomy without an operative scar in the neck is expected to improve patient satisfaction. We developed an original technique for performing endoscopic thyroidectomy using a breast approach and low pressure CO<sub>2</sub> insufflation into the subplatysmal space.<sup>9</sup>

The subcutaneous space in the breast area and subplatysmal space in the neck were bluntly dissected through a 15-mm incision between the nipples, and CO<sub>2</sub> was insufflated at 6 mmHg to create the operative space. Three trocars were inserted at the breast (Fig. 2), and dissection of the thyroid and division of the thyroid



**Fig. 2** Scarless endoscopic thyroidectomy: breast approach for better cosmesis.

vessels and parenchyma were performed endoscopically using an ultrasonic-activated scalpel. Four hemithyroidectomy and one partial resection of the thyroid for five female patients with thyroid adenomas 5 to 7 cm in diameter were successfully performed using this procedure. There were no conversions to open surgery or complications. No scars were apparent in the neck, and all patients were fully satisfied with the cosmetic results.

### **Development of Endoscopic Surgery for Esophageal Diseases**

The esophagus is anatomically hard to approach because it is surrounded by important organs, namely the trachea, bronchus, aorta, heart, lung, and so on. General thoracic surgeons are required to perform safe and sure operations on the esophagus. We also succeeded in the thoracoscopic or the laparoscopic treatment of esophageal diseases.<sup>10</sup>

#### *Thoracoscopic surgery*

The enucleation of an esophageal submucosal tumor, the resection of a giant esophageal diverticulum, and the resection of an esophagobronchial fistula were successfully performed by a full thoracoscopic procedure. Furthermore, patients with thoracic esophageal cancer were also treated thoracoscopically. The mobilization of the thoracic esophagus and the dissection of mediastinal lymph nodes were performed with better visualization.

#### *Laparoscopic Heller and Dor operation for esophageal achalasia*

Laparoscopic Heller myotomy and Dor fundoplication (Heller and Dor operation) is now regarded as the operation of the first choice for esophageal achalasia. It is indicated for patients who are resistant to medical therapy with a calcium blocker, for example, or have pneumatic dilatation and with frequent aspiration at night. Since it was reported that surgical treatment is better than pneumatic dilatation and since laparoscopic surgery is less invasive, the indications for the laparoscopic Heller and Dor operation could include all achalasia patients resistant to medical therapy. We successfully performed the laparoscopic Heller and Dor operation on 22 patients, all of whom had an uneventful postoperative course.<sup>11</sup> Manometric evaluation, endoscopic examination, and 24-hour pH monitoring showed good results. There are six important technical points: 1) flexible laparoscopy; 2) pneumoperitoneum; 3) gauze in the abdominal cavity to absorb blood; 4)

laparoscopic coagulating shears; 5) extra-corporeal knot-tying technique; and 6) intracorporeal knot-tying technique. If an experienced surgeon is in charge, the laparoscopic Heller and Dor operation is an ideal and minimally invasive treatment for esophageal achalasia.

#### *Laparoscopic Nissen fundoplication for gastro-esophageal reflux disease (GERD)*

Patients with gastroesophageal reflux disease were treated by laparoscopic Nissen fundoplication. Important technical points are similar to those of the laparoscopic operation for esophageal achalasia.

Patients were free from symptoms of heart burn without any medication postoperatively. The endoscopic examination revealed no esophagitis and the 24-hour pH monitoring demonstrated no significant gastroesophageal reflux. In addition, the upper GI series showed no reflux of contrast medium from the stomach to the esophagus in the Trendelenburg position.

### **Development of the Laparoscopic Surgery for Colorectal Diseases**

#### *Laparoscopic colectomy for colorectal cancer*

The argument of the application of laparoscopic surgery to the treatment of malignant diseases is mainly concerned with the expectation that lymph node dissection under laparoscopic manipulation would be less complete in comparison with that in open surgery. Since the systematic lymph node dissection procedure in colonic surgery is relatively simple compared with others including esophageal and gastric surgeries, colon cancer was the first candidate to evaluate the curability of the laparoscopic surgery against a malignant disease of the digestive organs.

We have applied laparoscopic surgery for the treatment of colorectal cancer since 1992, to early cancers in the first 4 years, and then up to advanced cancers based on the favorable results in the first application.<sup>12</sup> Even patients with lower rectal cancer were successfully treated by laparoscopic techniques with a satisfactory outcome in each.<sup>13</sup> Between June, 1992 and December, 2000, 372 patients with colorectal cancer underwent laparoscopic surgery in our institute. Among them, 274 patients (74%) had Dukes' A tumors, 48 (13%) Dukes' B, 45 (12%) Dukes' C, and 5 (1%) Dukes' D. Oral intake was started on median postoperative day 1, and median postoperative hospital stay was 8 days. Postoperative complications included wound sepsis in 18 (4.8%), anastomotic leakage in 13 (3.5%) and bowel obstruction in 9 (2.4%). Eleven patients developed recurrence (liver: 5, peritoneum: 3, local: 3). No port site recurrence was observed. The calculated 5-year survival

rate was 99.4% for Dukes' A, 100.0% for Dukes' B, and 82.6% for Dukes' C. Thus, it is suggested that laparoscopic surgery was technically feasible and oncologically sound in the treatment of colorectal cancer with favorable short- and long-term outcomes.<sup>14</sup>

Based on these results in the retrospective study, we conducted a randomized controlled trial to compare short-term outcomes of laparoscopic and open colectomy for advanced colorectal cancer.<sup>15</sup> Fifty-nine patients with T<sub>2</sub> or T<sub>3</sub> colorectal cancer excluding the transverse colon and rectum were randomized to undergo laparoscopic (n = 29) or open (n = 30) colectomy between June, 1998 and October, 2000. Operative time was longer (p < 0.001), while blood loss (p < 0.005) and postoperative analgesic requirement was less in the laparoscopic group than the open group. Earlier return of bowel motility and earlier discharge from the hospital (p < 0.05) were observed after laparoscopic surgery. Serum C-reactive protein levels on postoperative day 1 (p < 0.001) and 4 (p < 0.005) were lower in the laparoscopic group than the open group. No significant differences were found in leukocyte count, natural killer cell activity, and interleukin-6 levels between the two groups. Postoperative complications did not differ between the two groups. These results suggest that laparoscopic surgery for advanced colorectal cancer is feasible with favorable short-term outcome comparable to open surgery.

#### *Application for Crohn's disease*

Surgical treatment is often necessary for patients with Crohn's disease complicated by intestinal strictures or fistulas. We examined the technical feasibility in patients with Crohn's disease associated with strictures and fistulas.<sup>16</sup> Laparoscopic surgery was attempted in 37 patients with structuring ileal or ileocolonic Crohn's disease between 1994 and 2000 after failure of strict nutritional therapy. Twenty-four patients underwent ileocecal resection, 17 underwent strictureplasty, 15 partial resection of anastomotic recurrence. Oral intake was started a median of one day after the operation, and patients were discharged a median of 8 days after surgery. Six complications were observed in 41 surgeries (14.6%), including two intestinal obstructions/ileus, three wound infections, and one intraabdominal abscess. Two of these complications were associated with laparoscopic intracorporeal fistula takedown. There were no intraoperative or postoperative deaths. Four patients required conversion to open surgery (9.7%). Six patients who required reoperation for anastomotic recurrence underwent repeated laparoscopic surgery using the same small incision. It is suggested that laparoscopic treatment for Crohn's disease

complicated by fistulas is feasible, without high complication or conversion rates, and is applicable to reoperation for recurrent disease after laparoscopic treatment.

### **Development of Laparoscopic Surgery for Hepatobiliary Diseases**

#### *Laparoscopic clipless needle cholecystectomy*

Laparoscopic cholecystectomy has become the standard treatment for symptomatic cholelithiasis. Since 3 mm bipolar coagulation forceps and 2 mm instruments became available, our technique for laparoscopic cholecystectomy has changed. Bipolar energy never passes through the body, thus reducing any potential for conductive injury around the bile duct. Since the 3 mm bipolar coagulation can avoid using clips on the cystic duct and artery, the total cost of the procedure was reduced. Furthermore, the 2 mm and 3 mm incision sites can be closed easily in one minute by surgical tape without suturing. A 5-mm instrument is usually the acceptable size. However, 2 to 3 mm devices are more beneficial, leaving smaller scars. On the other hand, function of these instruments remains similar to the standard 5 mm instruments with the advancement of micro-technology. With the 2 mm instruments and 3 mm bipolar forceps, our standard technique for laparoscopic cholecystectomy became faster, less traumatic and less expensive.

We use the open laparoscopy method to place a 12 mm trocar through the umbilicus, and the abdomen is inspected using a flexible video laparoscope. One 3-mm trocar and two 2-mm trocars are placed in the abdomen under direct vision. These 2-mm instruments are stable enough for most lap-surgeries if a mini-port is used as a sheath to cover their weakness in rigidity. The 3-mm bipolar coagulation forceps and 2 mm mini-ties are used to coagulate and ligate the cystic artery and duct, so that clips for the artery and the duct will not be left in a patient's abdominal cavity. The clips left in the body have potential risks, such as migration or interference with possible future imaging of the hilum. This laparoscopic clipless needle cholecystectomy can be regarded as the optimum procedure for gall bladder removal.<sup>17</sup>

#### *Laparoscopic Liver Surgery*

Despite advances in laparoscopic techniques, laparoscopic liver surgery has not yet come into widespread use. However, we have accumulated patients with liver diseases since June, 1992, who underwent laparoscopic liver surgery including laparoscopic liver resection, laparoscopic/thoracoscopic microwave coagulating of the liver malignancies, laparoscopic deroofing of the liver cyst, and laparoscopic wedge biopsy of the liver.

Bleeding control, which is a basic element for liver surgery, needs to be better accessed by methods suitable for laparoscopic surgery in order to perform safer laparoscopic liver surgery. In our hospital, laparoscopic liver resections have been successfully performed by the application of the hilar blood flow control technique and automatic suturing devices. To establish a safer technique and the significance of laparoscopic liver surgery, we analyzed the initial results from the point of operative techniques and indications for laparoscopic liver surgery. Technical considerations for laparoscopic liver resection include intraoperative laparoscopic ultrasonography, abdominal wall lifting method, and the Pringle maneuver with a combination of several devices for hemostasis (microwave coagulator, laparoscopic coagulating shears, ultrasonic dissector, argon beam coagulator, bipolar electronic cautery and automatic suturing device). Patients with primary or metastatic liver tumors, who underwent laparoscopic resection or lap/thoracoscopic microwave coagulation, were seen during a four-year period at our hospital, and the results were found to be comparable with those of patients with these hepatic malignancies who underwent open liver resection during the same time period. The postoperative courses of these patients were uneventful. There were no postoperative bile leakage, bleeding (blood transfusion), or other complications. Postoperative hospital stay ranged from 4 to 8 days for laparoscopic liver resection. Thus, laparoscopic liver surgery can be safely performed and it can be well-established for certain hepatic diseases, although its indications remain restricted. For a safer laparoscopic liver resection, an abdominal wall lifting method is preferable in combination with an efficient bleeding control technique during parenchymal resection of the liver.<sup>18</sup>

### **Introduction of Robotics and Tele-communication Technologies to Endoscopic Surgery**

The application of the minimally invasive procedure to more complex operations requires new technology. Presently, a majority of abdominal operations can be done by the laparoscopic approach. However, there are major difficulties because the view of the operating field is restricted to a two-dimensional image, effector instruments have limited maneuverability due to the rigid shaft axis fixed to the abdominal wall by the entry trocar, and loss of direct contact with organs results in insufficient tactile information.

To overcome the difficulties of endoscopic manipulation, major research efforts have been devoted to develop a minimally invasive robotic surgery system that includes three-dimensional video imaging, tele-manipulated flexible effector instruments, and tactile

feedback. Current applications of robotics include progress in surgical assistance, image-guided therapy, and dexterity enhancement.<sup>19</sup>

#### *Robotic surgical assistance*

The idea of surgical assistance by robots is the creation of robotic devices that will allow surgeons to perform tasks that currently require more than one person. The robotic endoscope holder is an example of such device. Since the vision of the operating surgeon depends on the assistant responsible for holding and positioning of the endoscope in endoscopic surgery, a mis-directed and shakier image may be presented. To circumvent this problem, robotic endoscope holders have been developed which return direct control of the visual field to the operating surgeon, and hold the endoscope with greater stability offering the surgeon a stable image.

AESOP (Automated Endoscopic System for Optimal Positioning Computer Motion, Inc., Santa Barbara, Calif., USA) was the first commercial laparoscope positioning system introduced in 1994. We have used this robot clinically since 1996, and safely performed over 100 cases of 'solo-surgery' without human assistance. There were no disadvantages observed such as prolonged surgical duration, increased volume of operative bleeding, increased complication rate, or conversion to open surgery, in comparison with surgery with human assistance. Since a voice control human-machine-interface was developed, the robotic system has become more user-friendly.

#### *Master-slave manipulator*

Dexterity is enhanced by a master-slave manipulator in which a microprocessor is placed between the surgeons' hand (master) and the tip of the surgical instrument (slave). This system allows performance of superhuman tasks that cannot be done without computer enhancement.

Major advantages using master-slave manipulators are that the surgeon's tremor disappears at the robotic site, and that the surgeon can freely scale-down robotic movements. To date, several kinds of systems have already been introduced to the clinical practice. Among them, the da Vinci system (Intuitive Surgical, Inc, Mountain View, Calif., USA), equipped with two articulated joints at the tip which permits the system to have a total of 7 degrees of freedom and a high quality 3-D vision system, appears to provide superior dexterity to surgeons. We have introduced the da Vinci system to the laparoscopic surgery of gastrointestinal diseases since March, 2000 (Fig. 3), and confirmed the excellent maneuverability especially in suturing and



**Fig. 3** Operation using a master-slave manipulator.

ligating procedures. The surgeons can feel as if their miniature wrist and fingers are operating in the abdominal cavity. We confirmed in experiments of motion analysis that restrictions on the rotation of the surgeons' movements observed in the endoscopic manipulations can be relaxed using this system.<sup>1</sup> For example, taking advantage of this system, we have developed a novel method of cholecystectomy, where we ligated the cystic artery and cystic duct using strings to complete the procedure without leaving foreign bodies such as clips, and sutured the liver bed after resection of the gallbladder to repair defects of the peritoneum and prevent adhesion after surgery. We also succeeded in performing a complete endoscopic choledochojejunosotomy in a non-resectable advanced pancreatic cancer patient suffering from obstructed jaundice, which is currently performed by open surgery without this system. With research efforts devoted to such systems, the master-slave manipulators will be improved to carry out surgeries in a microscale or on moving organs through motion compensation.

The lack of tactile sensation, however, is the most serious demerit of current master-slave manipulators. It is one of the most difficult problems to overcome in the development of a robotic system. In the open air, we have developed a tele-presence system which transmits tactile sensations of remote objects using a PHANTOM (Personal Haptic Interface Mechanism) system (Sensible Technology, Inc, USA). Tactile sensations of the surface and elasticity of the remote object can be felt by the fingers as if they are really being touched, and even a delicate maneuver such as turning book pages can be done by tele-presence with complete tactile sensation. We expect this transmission system can be applied to the instruments of endoscopic surgery in the near future.

### *Surgical tele-mentoring*

Today, advanced tele-communication technology provides excellent motion images using only 3-ISDN (384 kb) telephone lines. Recently, the feasibility and efficacy of tele-consultation with some external partners during surgery has been demonstrated. Since endoscopic surgery is performed under video image, it is particularly suitable for tele-communication. We also constructed a tele-consultation system of endoscopic surgery between some collaborative urban hospitals, and developed a technique to tele-illustrate the color lines on video images bilaterally to increase the effectiveness of tele-consultation.<sup>17</sup> This annotation system considerably enhances the efficacy of surgical tele-consultation.

Experienced laparoscopic surgeons at collaborative hospitals have been able to successfully perform complex procedures by consulting specialists in laparoscopic surgery at our institute. Considering that the prices of tele-communicative devices are being reduced annually, and that the technological basis of the ISDN telephone system is simple and standardized, tele-consultation in endoscopic surgery should soon be available for routine clinical practice.

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