

## Initial Results of Robotic Surgery for Primary Lung Cancer: Feasibility, Safety and Learning Curve

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### ABSTRACT

**Background** At the end of 2016, robot-assisted thoracoscopic surgery (RATS) was still not covered by Japanese national health insurance. Therefore, few institutions in Japan perform RATS and even fewer have reported procedures as they occurred earlier. So, we decided to focus on the initial results of RATS for primary lung cancer.

**Methods** We retrospectively reviewed 44 patients who underwent RATS for primary lung cancer from January 2011 to August 2016. After mastering the initial procedure, we introduced a completely portal robotic pulmonary resection procedure using a carbon dioxide insufflation system. Cases were divided into 2 groups: the early period (20 cases) and the later period (24 cases).

**Results** There was no case of conversion to video-assisted thoracoscopic surgery or thoracotomy. In the 44 cases of primary lung cancer, median operating time was 239.5 min, console time was 179 min, blood loss was 10 mL, drainage period was 2 days, morbidity of Grade 2 or more (Clavien-Dindo classification) was 18.2%, morbidity of Grade 3 or more was only 4.6%, and there was no 30-day mortality. Median operating and console times were significantly shorter in the later period (215 min and 159.5 min, respectively) than in the initial period (300.5 min and 228 min, respectively). Median blood loss was significantly lower in the later period (5 mL) than in the initial period (50 mL). Five-year overall and disease-free survival rates were 100% and 88.9%, respectively.

**Conclusion** RATS for primary lung cancer is feasible and safe, has a faster learning curve, and provides satisfactory. Studies with longer follow-ups and larger numbers of cases are necessary.

**Key words** initial results; primary lung cancer; robotic surgery

Robot-assisted thoracoscopic surgery (RATS) for lung cancer was first reported by Melfi et al. in 2002.<sup>1</sup> Since then, RATS for lung cancer has become widely adopted, centering in Europe and North America. In Japan, the Pharmaceutical Affairs Council of the Ministry of Health, Labour and Welfare approved the da Vinci S Surgical System (Intuitive Surgical, Sunnyvale, CA) in November 2009, followed by the da Vinci Si Surgical System (Intuitive Surgical) in October 2012. In 2010, Suda et al.<sup>2</sup> performed the first case of RATS lobectomy for lung cancer in Japan. We began performing RATS for general thoracic surgery (lung cancer and mediastinal disease) in January 2011, and reported on the procedures in 2012.<sup>3</sup> Furthermore, the initial results of 60 cases of RATS for lung cancer in 9 institutions in Japan were reported in 2014.<sup>4</sup> However, at the end of 2016, RATS was still not covered by Japanese national health insurance. Therefore, few institutions in Japan perform RATS, and even fewer have reported the initial results. Here, we report the initial results of RATS for primary lung cancer at a single institution, and compare the perioperative outcomes of the early period with those of the later period.

### SUBJECTS AND METHODS

#### Patients and data collection

We performed RATS for 45 lung cancer patients using the da Vinci S or Si Surgical System from January 2011 to August 2016 at our hospital. However, one case was diagnosed as metastatic lung tumor from ovarian cancer, histologically. Thus, we retrospectively analyzed 44 patients who underwent RATS for primary lung cancer.

There were 17 men and 27 women with a median age of 70.0 years (range, 39–83 years). According to the 7th edition of the TNM classification,<sup>5</sup> all cases were clinical N0, and 43 cases were clinical stage I. One case was clinical stage II because of T3 classification. However, the number of cases of pathologic stage I decreased to 38. The most common histologic type was adenocarcinoma (40 cases). Standard lobectomy was performed

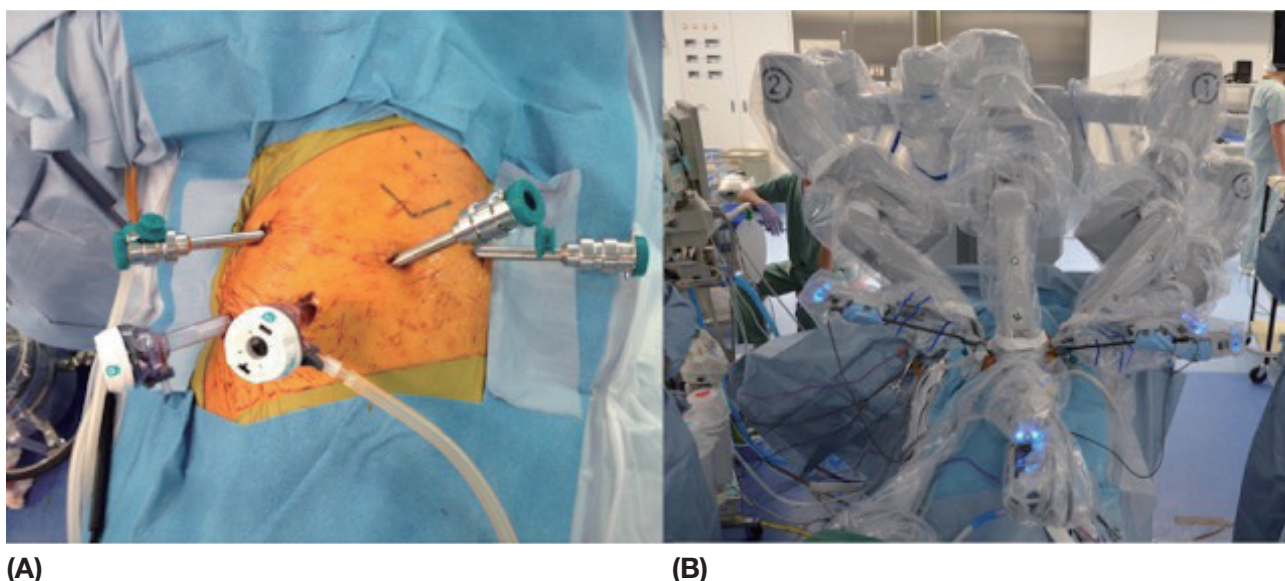
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Abbreviations: CPRL, completely portal robotic pulmonary resection; RATS, robot-assisted thoracoscopic surgery; VATS, video-assisted thoracoscopic surgery



**Fig. 1.** Standard trocar placement (A) and the photo of docking with the robotic arms (B) for completely portal robotic pulmonary resection with 4 arms using a carbon dioxide insufflation system.

in 42 cases (95%), comprised of 20 right upper lobectomy (including 1 case of bronchoplasty), 6 right middle lobectomy, 4 right lower lobectomy, 7 left upper lobectomy, and 5 left lower lobectomy. Segmentectomy was performed in 2 cases, comprised of including the left upper segmentectomy and left basal segmentectomy.

Patients who underwent RATS for primary lung cancer were divided into 2 groups: the early period (before the 20th case) and the later period (after the 21st case). The study protocol was approved by the Institutional Review Board of Tottori University Faculty of Medicine (Approval No. 1528), and informed consent was obtained from each patient before operation. Perioperative outcomes and survival data were analyzed. Morbidity, defined as postoperative complication within 30 days after surgery, was classified according to the Clavien-Dindo classification system.<sup>6</sup>

#### Operative indication and surgical technique

The indications for RATS for primary lung cancer were the same as stage I non-small-cell lung cancer in accordance with video-assisted thoracoscopic surgery (VATS) lobectomy and segmentectomy.

Our robotic operative technique has been described previously.<sup>3</sup> First port was placed in the seventh or eighth intercostal space along the mid-axillary line for the camera (12 mm, 30° angled down scope). The other 8-mm da Vinci trocars were placed in the fifth intercostal space along the anterior-axillary line (for the second arm), seventh intercostal space along the posterior-axillary line (for the third arm), and seventh intercostal space on the posterior side of the tip of the scapula (for

the fourth arm). More than 8 cm of distance between each robotic port was required. A utility port for the assistant surgeon was placed in the fifth intercostal space along the anterior-axillary line or used the same incision for the fourth arm. We performed RATS using 3 arms initially, and introduced the fourth arm from the 11th case. Furthermore, we introduced a completely portal robotic pulmonary resection (CPRL) technique<sup>7</sup> using a CO<sub>2</sub> insufflation system with pressure setting at 5 to 10 mmHg from the 28th case (Fig. 1).

#### Statistical analyses

Comparisons between groups were performed using the chi-squared test for categorical data, and the Mann-Whitney *U* test for nonparametric data. Survival was calculated using the Kaplan-Meier method. All statistical analyses were performed using StatView 5.0J (SAS Institute, Cary, NC). A *P* value of 0.05 was considered significant.

## RESULTS

#### Perioperative outcomes of all patients who underwent RATS for primary lung cancer

There was no case of conversion to VATS or open thoracotomy. Median operating time was 239.5 min, console time was 179 min, blood loss was 10 mL, drainage period was 2 days, morbidity of Grade 2 or more (Clavien-Dindo classification) was 8 cases (18.2%), morbidity of Grade 3 or more was 2 cases (4.5%), comprised of chylothorax and cholecystitis. There was no 30-day mortality.

### Comparison of perioperative outcomes between the early period and the later period of patients who underwent RATS for primary lung cancer

Table 1 shows the characteristics between the early period (20 cases) and the later period (24 cases) of the patients who underwent RATS for primary lung cancer. There were no significant differences in gender, age, clinical stage, histology, pathologic stage, and surgical procedure between periods. Table 2 shows the perioperative outcomes between the early period and the later period. Operating time was significantly shorter in the later period (median, 215 min) than in the early period (median, 300.5 min) ( $P = 0.0001$ ). Console time also was significantly shorter in the later period (median,

159.5 min) than in the early period (median, 228 min) ( $P < 0.0001$ ). Moreover, blood loss was significantly lower in the later period (median, 5 mL) than in the early period (median, 50 mL) ( $P = 0.008$ ). However, there were no significant differences in drainage period, morbidity of Grade 2 or more and respiratory morbidity of Grade 3 or more between periods.

### Survival of patients who underwent RATS for primary lung cancer

At a median follow-up of 34.5 months (range, 1–67 months), all 44 patients who underwent RATS were alive, while 4 patients experienced recurrence. Recurrence site was pleural and pulmonary metastasis in 1 case, pulmonary metastasis in 1, pleural and bone metastasis in 1, and trachea-bronchus recurrence in 1 (bronchoplastic right upper lobectomy, 65-month disease-free period). Five-year overall and disease-free survival rates were 100% and 88.9%, respectively (Fig. 2).

### DISCUSSION

The main reasons that RATS has not become widely adopted in Japan seem to be problems with national health insurance and cost.<sup>4</sup> Additionally, there are some risk-benefit problems characteristic of the thoracic organs in the general thoracic surgery field: i) numerous great vessels with abundant blood flow are present in the thoracic cavity; ii) the target area is wide; iii) the main procedure is resection, and reconstruction procedures are limited; iv) only limited institutions have introduced complete thoracoscopic surgery; and v) the learning curve is slower than that in other fields.<sup>8</sup>

In this study, regarding perioperative outcomes, there was no case of conversion to VATS or open thoracotomy, morbidity of Grade 3 or more was only 4.6%, and no 30-day mortality. The learning curve was 20 cases.

RATS for lung cancer was introduced with low

**Table 1. Patient characteristics between the early period and the later period**

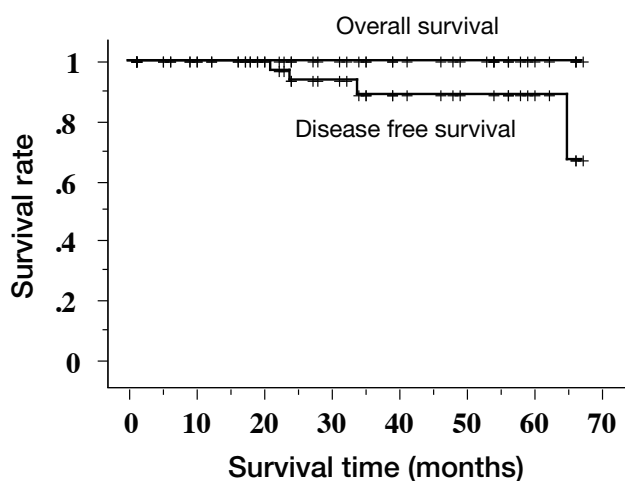
	Early period	Later period	<i>P</i> value
No. of cases	20	24	
Gender			0.87
Male	8	9	
Female	12	15	
Age, median (y)	74 (39–83)	66.5 (59–80)	0.47
Clinical stage			0.65
IA	13	15	
IB	7	8	
IIB	0	1	
Histology			0.85
Adenocarcinoma	18	22	
Squamous cell carcinoma	2	2	
Pathologic stage			0.81
IA	11	15	
IB	6	6	
IIA	2	1	
IIB	1	1	
IIIA	0	1	
Surgical procedure			0.89
Lobectomy (including bronchoplasty 1)	19	23	
Segmentectomy	1	1	

No., number; y, year(s).

**Table 2. Perioperative outcomes between the early period and the later period**

	Early period	Later period	<i>P</i> value
No. of cases	20	24	
Operating time, median (min)	300.5 (208–555)	215 (120–304)	0.0001
Console time, median (min)	228 (157–400)	159.5 (72–221)	< 0.0001
Blood loss, median (mL)	50 (5–200)	5 (5–350)	0.37
Drainage period, median (d)	2 (1–4)	2 (2–10)	0.73
Morbidity* ( $\geq$ G2), (%)	3 (15.0)	5 (20.8)	0.62
Respiratory morbidity* ( $\geq$ G3), (%)	0 (0)	1 (4.2)	0.36

\*Clavien-Dindo classification. No., number.



**Fig. 2.** Survival curves of patients who underwent robotic surgery for primary lung cancer.

rates of morbidity (6.7%–43.8%) and mortality (0%–0.4%).<sup>4, 7, 9–11</sup> In this study, morbidity and mortality rates were 18.2% and 0%, respectively, demonstrating that RATS for lung cancer was safely introduced at our institution. In a previous study, Kent et al.<sup>10</sup> compared the perioperative outcomes between RATS, VATS, and open thoracotomy procedures for lung cancer using propensity-matched analysis based on data from the state inpatient database. They reported that RATS was associated with significant reductions in mortality, length of hospital stay, and overall complication rates when compared with open thoracotomy, but that none of these differences were significant when compared with VATS. Paul et al.,<sup>12</sup> using a nationwide inpatient sample, reported that RATS lobectomy was associated with higher rates of intraoperative injury and bleeding compared with VATS lobectomy. On the other hand, Farivar et al.,<sup>11</sup> using comparative analysis based on data from the Society of Thoracic Surgeons national database, suggested the potential benefits of RATS relative to VATS and open thoracotomy for lung cancer, particularly reduced length of hospital stay, mortality, and postoperative blood transfusion. Therefore, the evidence is still inconclusive whether RATS is more useful than VATS for lung cancer with regard to perioperative outcomes. Previous studies demonstrated that operating time of RATS for lung cancer was longer than that of VATS for lung cancer.<sup>13, 14</sup> However, Veronesi<sup>15</sup> reported that the learning curve of RATS lobectomy (number of operations required, 6–20) was shorter than that of VATS lobectomy (number of operations required, 25–50). In our study, operating and console times were significantly shorter after around 20 cases. Thus, our data seem to support Veronesi's idea.

Regarding CPRL, Melfi et al.<sup>16</sup> reported that RATS

for lung cancer using 4 arms and CO<sub>2</sub> insufflation is effective in terms of perioperative outcomes, including operating time and rates of conversion, mortality, and morbidity. We believe that CPRL with CO<sub>2</sub> insufflation is useful to widen the working space of robotic forceps. Furthermore, Nasir et al.<sup>17</sup> referred to the possibility that CPRL with CO<sub>2</sub> insufflation might prevent tissue desiccation and further inflammation in the chest. As for CO<sub>2</sub> pressure, previous studies reported that RATS should be performed using 10 mmHg or less.<sup>7, 16</sup> Moreover, Wolfer et al.<sup>18</sup> proposed that low-pressure (< 10 mmHg) insufflation is a safe adjunct to the conduct of routine thoracoscopic surgical procedures, because central venous pressure significantly increases at 14 mmHg. Therefore, we introduced CPRL using a CO<sub>2</sub> insufflation system with pressure setting at 5 to 10 mmHg. There is a possibility that CPRL with CO<sub>2</sub> insufflation influenced the significantly lower blood loss in the later period on our study.

As for the long-term survival after RATS, there are few reports.<sup>19, 20</sup> Park et al.<sup>19</sup> reported a multicenter study involving 325 patients, in which the 5-year survival rate in all patients was 80% (stage IA, 91%; stage IB, 88%; stage II, 49%). Recently, Yang et al.<sup>20</sup> reported the long-term survival of 172 patients who underwent RATS lobectomy for clinical stage I lung cancer, in which the 5-year overall and disease-free survival rates were 77.6% and 72.7%, respectively. Our results were more favorable in spite of small series and short follow up time.

We performed RATS bronchoplastic right upper lobectomy as it was reported previously.<sup>21</sup> For sleeve or bronchoplastic lobectomy, some reports also have described one of the great advantage of RATS.<sup>22, 23</sup> Besides this, some reports have described the usefulness of RATS for lymph node dissection.<sup>24, 25</sup> However, regarding its usefulness and advantages, almost all reports cited so far included limited numbers of cases, were retrospective studies, and/or conducted propensity-matched analyses, and there are very few prospective randomized trials. Recently, it was reported that a prospective, randomized, multicenter trial (NCT02804893) to compare the complications and conversion rates between RATS and VATS approaches for stage I and II lung cancer have just begun.<sup>26</sup> We will expect the beneficial results of this randomized trial.

In the present study, of course there are several limitations: single-institution, nonrandomized, retrospectively analyzed cohort of patients, the most obvious being a selection bias. This study also did not analyze the influence of CPRL with CO<sub>2</sub> insufflation. However, when considering the current state that RATS is not covered by Japanese national health insurance, we believe

there is a significance of this retrospective study.

In conclusion, RATS for lung cancer is feasible and safe, has a faster learning curve, and provides satisfactory initial results. However, studies with longer follow-up and larger numbers of cases are necessary. Prospective studies showing favorable result of RATS are mandatory for coverage by Japanese national health insurance.

*The authors declare no conflict of interest.*

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