

## Takao Hiraki's work on interventional radiology

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**Figure 1** Takao Hiraki, MD, Assistant Professor, Department of Radiology, Okayama University Medical School, Shikatacho 2-5-1, Okayama 700-8558, Japan.

### Abstract

Dr. Takao Hiraki is a scientist carrying out interventional radiology research in the Department of Radiology at Okayama University Medical School, Japan. He has conducted animal and human clinical studies on interventional radiology for various conditions. For example, he clarified the hepatic hemodynamic changes caused by hepatic venous occlusion. He also developed new devices, such as hydrogel coils for the occlusion of the aneurismal sac after an endovascular stent-graft of an aortic aneurysm to prevent endoleakage and small intestinal submucosa-covered stents for transjugular intrahepatic portosystemic shunts. Further, he performed a number of studies on the radiofrequency ablation of lung cancer, mediastinal lymph node metastasis, and computed tomography-fluoroscopy-guided lung biopsies. He intends to continue to dedicate his academic career to expand the role of interventional radiology in clinical medicine.

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**Key words:** Radiology; Interventional radiofrequency ablation; Lung cancer; Computed tomography fluoroscopy; Lung biopsy; Hepatic hemodynamics; Pneumothorax; Mediastinal lymph node metastasis

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### INTRODUCTION AND EDUCATIONAL EXPERIENCE

Dr. Takao Hiraki (Figure 1) was born in February 1971 and aspired to become a medical doctor at an early age. He received his medical degree from Okayama University Medical School in Japan in 1995. He embarked upon his scientific career in the Department of Radiology at Okayama University Medical School by clarifying the hepatic hemodynamic changes caused by hepatic venous occlusion with Doppler sonography in 2001<sup>[1]</sup>. In 2002, Dr. Hiraki worked as a research fellow in the Dotter Interventional Institute, Oregon, USA and carried out various animal studies on interventional radiology<sup>[2-5]</sup>, developing new devices such as hydrogel coils for occlusion of the

aneurysmal sac after the endovascular stent-graft of an aortic aneurysm to prevent endoleakage and small intestinal submucosa covered stents for transjugular intrahepatic portosystemic shunts. He returned to Japan in 2004 and was employed as a clinician in the Department of Radiology at Okayama University Medical School. Since then, he has performed a number of animal and human clinical studies, mainly focusing on nonvascular interventional radiology<sup>[6-31]</sup>.

He has received various awards from the Japanese Society of Interventional Radiology, Japan Radiological Society, and Okayama Medical Association for his outstanding academic achievements. In addition, he has been an invited speaker at international meetings, and is a peer reviewer for a number of international scientific journals, such as *Lancet Oncology*, *Cancer*, *Journal of Vascular and Interventional Radiology*, and *Cardiovascular and Interventional Radiology*. He has been an editorial board member of the *World Journal of Radiology* since 2009.

## ACADEMIC ACHIEVEMENTS

### **Hepatic hemodynamic change induced by hepatic venous occlusion**

Although it has been well known that characteristic findings on hepatic arteriography are observed in patients with primary or secondary Budd-Chiari syndrome, the hepatic hemodynamic changes induced by hepatic venous occlusion were poorly understood. Dr. Hiraki and his coworkers clarified these altered hepatic hemodynamics by hepatic venous occlusion with the use of Doppler ultrasonography<sup>[1]</sup>.

Extracorporeal ultrasonography and a transducer-tipped guide wire were used to evaluate the hemodynamics of the portal vein and hepatic artery, respectively. Such hemodynamics were evaluated before and after balloon occlusion of the right hepatic vein. The maximum peak velocity of the right portal vein was significantly decreased with occlusion. In the majority of cases, hepatic venous occlusion changed the Doppler signal in the portal venous branch of the occluded area from hepatopetal to no signal. The average peak velocity of the right hepatic artery showed a decrease or plateau for 15-30 s after the start of occlusion and then rapidly increased to reach a plateau at approximately 75-90 s with 1.5-2 times higher velocity than before the occlusion. Such altered hepatic hemodynamics are thought to enhance the effect of interventional therapies. Increased hepatic arterial flow may lead to higher concentrations of chemotherapeutic agents during transcatheter chemoembolization; furthermore, decreased portal flow may increase the coagulation volume during radiofrequency (RF) ablation.

### **Percutaneous RF ablation of mediastinal lymph node metastasis**

Hiraki *et al*<sup>[6]</sup> were the first to perform RF ablation of mediastinal lymph node metastasis. It is quite challenging to perform RF ablation of the mediastinal lymph node

because the mediastinum is relatively crowded with major vessels and the trachea. In all of the 7 cases examined, the electrode was successfully inserted into the target lymph node without damaging major vessels. As all of the treated lymph nodes were directly adjacent to the trachea, the trachea was protected from thermal damage by using a balloon filled with chilled saline that was introduced into the trachea at the level of the lymph node. RF ablation was carried out while monitoring the temperature of the tracheal mucosa by using a thermocouple attached to the balloon. Three of the 7 lymph node metastases were locally controlled with 1 or 2 ablation sessions, and thermal damage of the trachea was avoided in 5 of the 7 cases. This preliminary study was considered to have made a substantial impact on the use of RF ablation in the mediastinum.

### **Percutaneous RF ablation of lung cancer**

**Local tumor control:** Hiraki *et al*<sup>[7]</sup> clarified local tumor control and the affecting factors. Their preliminary study showed that the local control rates of 342 tumors were 72% at 1 year, 60% at 2 years, and 58% at 3 years. Larger tumors and the use of an internally cooled electrode were revealed as independent risk factors for local failure<sup>[7]</sup>. When a 2-cm diameter array of multitined expandable electrodes was expanded at the center of tumors that were  $\leq 1$  cm and separate from the bronchus, local control was 96%<sup>[8]</sup>.

Besides tumor size and electrode type, tumor type may also affect the local control outcomes because of varying tumor characteristics related to cytology, pathophysiology, and biology. Hiraki *et al*<sup>[9]</sup> evaluated the local control outcomes of 5 types of cancer: primary lung cancer and pulmonary metastases from colorectal cancer; lung cancer; renal cell carcinoma; and hepatocellular carcinoma. The overall local control rates were 86% and 76% at 1 and 2 years, respectively. According to univariate analysis, metastatic colorectal cancer showed significantly higher local control rates than the other 4 types of cancer. However, multivariate analysis, by which various factors significantly affecting local tumor control can be adjusted among the 5 tumor types, indicated that the relative risk of local progression for a given tumor type was comparable to the risks for the other 4 types. This result indicated that RF ablation may provide similar local efficacy, independent of tumor type.

The notable advantage of RF ablation may be the ability to repeat the procedure in case of local failure. Hiraki *et al*<sup>[10]</sup> were successful in clarifying that repetition of the procedure significantly improved local control outcomes. The aorta and the heart are substantial obstacles when performing RF ablation for tumors that are located near these structures. Dr. Hiraki and his coworkers showed that while the procedure may be safely performed for these tumors, local efficacy was quite limited with a local control rate of 9%<sup>[11]</sup>.

**Patient survival:** Hiraki *et al*<sup>[12]</sup> clarified patient survival

after RF ablation in the lung. For 20 nonsurgical candidates (11 males and 9 females; mean age, 75.6 years) with clinical stage I (IA,  $n = 14$ ; IB,  $n = 6$ ) non-small cell lung cancer, the overall survival rates were 90% at 1 year, 84% at 2 years, and 74% at 3 years; the cancer-specific survival rates were 100% at 1 year, 93% at 2 years, and 83% at 3 years with a mean survival time of 42 mo. As for pulmonary metastases from colorectal cancer, the survival rates after RF ablation were 96% at 1 year, 54% at 2 years, and 48% at 3 years during a median follow-up period of 20.1 mo for 27 patients (19 males and 8 females; mean age, 61.6 years)<sup>[13]</sup>. A significant prognostic factor was the presence of extrapulmonary metastasis<sup>[13]</sup>.

With regard to pulmonary metastases from hepatocellular carcinoma, Hiraki *et al*<sup>[14]</sup> reported two very promising cases of long-term survival after RF ablation for pulmonary metastasis. Further, they performed a multicenter study to investigate survival after pulmonary metastases from hepatocellular carcinoma<sup>[15]</sup>. For 32 patients (24 males and 8 females; mean age, 61.9 years), the overall survival rates were 87% at 1 year and 57% at 2 and 3 years during a median follow-up period of 20.5 months<sup>[15]</sup>. Significantly better survival rates were obtained for patients with an absence of viable intrahepatic recurrence, Child-Pugh grade A, absence of liver cirrhosis, absence of hepatic C virus infection, and  $\alpha$ -fetoprotein levels  $\leq 10$  ng/mL at the time of RF ablation<sup>[15]</sup>.

**Complications:** Pneumothorax is the most common complication following RF ablation. Hiraki *et al*<sup>[16]</sup> evaluated pneumothorax after the RF ablation of lung cancer. The incidence of pneumothorax and chest tube placement for pneumothorax following RF ablation was 52% and 21%, respectively. Risk factors for pneumothorax included male gender, no history of pulmonary surgery, a greater number of tumors ablated, involvement of the middle or lower lobe, and increased length of the aerated lung traversed by the electrode<sup>[16]</sup>.

Although the vast majority of pneumothorax can be treated conservatively or *via* the placement of a chest tube, air leakage rarely persisted despite chest tube placement. Dr. Hiraki and his coworkers reported 2 cases of such intractable pneumothorax caused by the development of a bronchopleural fistula<sup>[18]</sup>. Dr. Hiraki and coworkers also investigated the relationship between pleural temperature and pleural events (e.g. pneumothorax and pleural effusion) after the RF ablation of lung tumors. The occurrence of pleural effusion was shown to be associated with higher pleural temperatures during the procedure, whereas pneumothorax was not related to pleural temperature<sup>[18]</sup>.

Dr. Hiraki and coworkers also reported rare but important complications following lung RF ablation: 2 cases of needle-tract seeding<sup>[19]</sup>; 4 cases of brachial nerve injury<sup>[20]</sup>; 1 case of pulmonary artery pseudoaneurysm<sup>[21]</sup>; and 1 case of *Aspergillus* infection<sup>[22]</sup>.

**Attempts to enhance the efficacy of RF ablation:** In an attempt to enhance the local efficacy of RF ablation in

the lungs, Dr. Hiraki and his coworkers conducted studies on animal models<sup>[23,24]</sup>. They noted a heat sink effect in the pulmonary artery and performed RF ablation after pulmonary artery embolization. Pulmonary artery embolization significantly increased coagulation size<sup>[23]</sup>. Dr. Hiraki and his coworkers also noted that alveolar air was an obstacle to ablation because air has limited electrical and thermal conductivity. They infused saline into the lung parenchyma, resulting in significantly enlarged coagulation<sup>[24]</sup>.

In the clinical setting, Dr. Hiraki and his coworkers completely treated a 4.7 cm hypervascular metastasis from hepatocellular carcinoma that was in contact with the pulmonary hilum<sup>[25]</sup>. Transcatheter embolization, then RF ablation, and lastly external beam radiation were applied for the treatment of the tumor. Considering that it was a large hilar tumor, the successful result indicated the synergistic effect of embolization and radiation on the efficacy of RF ablation.

**Percutaneous computed tomography fluoroscopy-guided lung biopsy:** Although conventional computed tomography (CT)-guided needle biopsy is an established diagnostic tool for pulmonary lesions, few large studies have clarified the diagnostic outcomes of the procedure using CT fluoroscopy. Thus, Dr. Hiraki and his coworkers conducted a retrospective study on the diagnostic outcomes of 1,000 CT fluoroscopy-guided lung biopsies performed with 20-gauge coaxial cutting needles<sup>[26]</sup>. The biopsy results were nondiagnostic in 0.6% of the lesions. The sensitivity and specificity for the diagnosis of malignancy was 94% and 99%, respectively, while diagnostic accuracy was 95%. The significant independent risk factors for diagnostic failure were as follows: the acquisition of 2 or fewer specimens; lesions in the lower lobe; malignant lesions; and lesions  $< 1.0$  cm and  $> 3.1$  cm. It was notable that the diagnostic accuracy reached 93% even for lesions  $< 1.0$  cm. This surprising result was suggested to depend on the use of CT fluoroscopy.

Dr. Hiraki and coworkers also clarified that CT fluoroscopy-guided lung biopsy was useful for the correct diagnosis of lesions for which bronchoscopy-guided biopsy gave false negative results<sup>[27]</sup>. Further, a high diagnostic yield by CT fluoroscopy-guided lung biopsy was observed for pure ground glass opacity lesions, with a sensitivity of 95%, specificity of 100%, and diagnostic accuracy of 95%<sup>[28]</sup>.

Dr. Hiraki and his coworkers also evaluated the complications following CT fluoroscopy-guided lung biopsy. First, they clarified that the overall incidence of pneumothorax after 1098 CT fluoroscopy-guided lung biopsies was 42% and chest tube placement was required in 12% of pneumothoraces<sup>[29]</sup>. The significant independent risk factors for pneumothorax were no prior pulmonary surgery, lesions in the lower lobe, greater lesion depth, and a needle trajectory angle of  $< 45^\circ$ ; those for chest tube placement for pneumothorax were pulmonary emphysema and greater lesion depth<sup>[29]</sup>. Attention should be paid to patients with a congenital pericardial defect because pneumothorax may result in pneumopericardium<sup>[30]</sup>.

Systemic air embolism is a rare but potential fatal complication following a percutaneous lung biopsy. Dr. Hiraki and his coworkers reported 4 cases of systemic air embolism following a CT fluoroscopy-guided lung biopsy<sup>[31]</sup>. They observed that the incidence of systemic air embolism was 0.4%. All patients experienced paroxysms of coughing during the procedure. In 3 patients without cardiac or cerebral symptoms, the presence of systemic air was confirmed on postprocedural CT scan images; it was resolved after immediate therapy without causing morbidity. The presence of systemic air was missed in 1 initially asymptomatic patient, resulting in a subsequent neurologic deficit. Considering that the number of reports on this complication is increasing in proportion to increased awareness, the true incidence is probably much higher than expected. Dr. Hiraki and his coworkers are currently conducting a multicenter study to analysis the risk factors for this complication. The results of this study will help to understand its etiology and to design prophylaxis against it.

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