**TABLE 1.** Second Primary Cancer Patients With/Without CT Scan Before the Diagnosis of Pancreatic Cancer

| AJCC Stage | With CT Scan | Without CT Scan | Total |
|---|---|---|---|
| IA | 1 (7.7%) | 1 (3.8%) | 2 (5.1%) |
| IB | 0 | 2 (7.7%) | 2 (5.1%) |
| IIA | 2 (15.4%) | 2 (7.7%) | 4 (10.2%) |
| IIB | 6 (46.2%) | 7 (26.9%) | 13 (33.3%) |
| III | 0 | 1 (3.8%) | 1 (2.6%) |
| IV | 4 (30.8%) | 13 (50%) | 17 (43.5%) |
| Total | 13 (100%) | 26 (100%) | 39 (100%) |

AJCC indicates American Joint Committee on Cancer.

detected after diagnosis of pancreatic cancer, with a median time interval of 0.5 years (range, 0.2–0.8 years).

In the present study, the highest rate of multiple malignancies was recorded in patients with gastric cancer, followed by colorectal and hepatocellular cancers as the second and third highest multiple cancers. The increased incidence of these cancer types in Korea may explain the high proportion of multiple cancers. The gastric cancer incidence rate in Korea (40.4 per 100,000) is the highest in the world, and within Korea, colorectal and hepatocellular cancers are the third and fourth most common cancers.[7] In order of decreasing incidence, gastric, colorectal, hepatocellular, bladder, and gallbladder cancers are common multiple cancers. The primary risk factor for bladder cancer is cigarette smoking. Shen et al[8] showed a significant increase in the standardized incidence ratio of pancreatic cancer among both women and men after pharynx, larynx, stomach, bladder, and cervical cancers. In addition to the common environmental traits with this association, chemicals and occupational exposure, particularly medical conditions of the gallbladder, including gallstones, cholecystectomy, and cholecystitis, may be shared determinants.[9]

Improved cancer therapies and resulting enhancement of survival may increase the risk of a therapy-induced second primary malignant neoplasm. In a previous study, the standardized incidence ratio of pancreatic cancer was significantly increased after 10 years of diagnosis of cancers of the stomach, colon, gallbladder, breast, cervix uteri, placenta, corpus uteri, ovary, testis, bladder, kidney, and eye, as well as Hodgkin and non-Hodgkin lymphomas.[8] A lengthy latency period is believed to be necessary for the promotion of new malignant neoplasms by therapeutic factors.

In the present study, CT findings suspicious for pancreatic cancer were observed in 7 patients (54%) before pancreatic cancer diagnosis. Typically, pancreatic cancer appears on a contrast-enhanced CT scan as an ill-defined, hypoattenuating focal mass with dilation of the upstream pancreatic duct.[10] Although CT scan as a screening method of early detection for pancreatic cancer is not recommended for the general population or asymptomatic subjects, its use for early detection of pancreatic cancer in other cancer patients has been reported.[5] Computed tomography can be used to detect a significant proportion of asymptomatic incident pancreatic cancers before clinical diagnosis. The presence of focal hypoattenuation and pancreatic duct dilatation are useful findings associated with the diagnosis of pancreatic cancer and are detectable on CT scan with a high degree of reproducibility.[5] In the current study, the proportion of stage III to IV pancreatic cancers was lower in patients subjected to the CT scan than those without the CT scan, but the data did not reach statistical significance. Further studies are thus required to determine the effectiveness of CT use for pancreatic cancer detection in a high-risk population.

In conclusion, cancers of the gastrointestinal tract and hepatobiliary system are often associated with pancreatic cancer in patients with multiple primaries in Korea. A significant proportion of incident pancreatic cancers can be detected in prediagnostic CT scans for follow-up evaluation of nonpancreatic cancer.

## ACKNOWLEDGMENT

*The authors declare no conflict of interest. The authors have no funding to disclose. Drs Han and Oh contributed equally to this work.*

**Mi Ah Han, MD**
National Cancer Control Institute
National Cancer Center
Goyang, Republic of Korea
Department of Preventive Medicine
College of Medicine
Chosun University
Gwangju, Republic of Korea

**Myueng Guen Oh, MD**
Center for Liver Cancer
National Cancer Center
Goyang, Republic of Korea
Department of Internal Medicine
Haengchon Medical Foundation
Haenam General Hospital
Haenam, Republic of Korea

**Sang Myung Woo, MD**

**Woo Jin Lee, MD, PhD**

**Sang-Jae Park, MD, PhD**

**Sung-Sik Han, MD, PhD**

**Young Hwan Koh, MD, PhD**

**Tae Hyun Kim, MD, PhD**

**Eun Kyung Hong, MD, PhD**
Center for Liver Cancer
National Cancer Center
Goyang, Republic of Korea
wsm@ncc.re.kr

**Sohee Park, PhD**
Division of Cancer
Registration and Surveillance
National Cancer Center
Goyang, Republic of Korea

**Joong-Won Park, MD, PhD**

**Chang-Min Kim, MD, PhD**
Center for Liver Cancer
National Cancer Center
Goyang, Republic of Korea

## REFERENCES

1. Boice J Jr, Storm H, Curtis R, et al. Introduction to the study of multiple primary cancers. *Natl Cancer Inst Monogr.* 1985;68:3.
2. Neugut A, Robinson E. Multiple primary neoplasms. *Cancer J.* 1992;5:245–248.
3. Kobayashi Y, Arimoto H, Watanabe S. Occurrence of multiple primary cancer at the National Cancer Center Hospital, 1962–1989. *Jpn J Clin Oncol.* 1991;21:233.
4. Schenker JG, Levinsky R, Ohel G. Multiple primary malignant neoplasms in breast cancer patients in Israel. *Cancer.* 1984;54:139–144.
5. Ahn SS, Kim MJ, Choi JY, et al. Indicative findings of pancreatic cancer in prediagnostic CT. *Eur Radiol.* 2009;19:2448–2455.
6. Parkin D, Pisani P, Lopez A, et al. At least one in seven cases of cancer is caused by smoking. Global estimates for 1985. *Int J Cancer.* 1994;59:494–504.
7. Jung K, Park S, Kong H, et al. Cancer statistics in Korea: incidence, mortality and survival in 2006–2007. *J Korean Med Sci.* 2010;25:1113–1121.
8. Shen M, Boffetta P, Olsen J, et al. A pooled analysis of second primary pancreatic cancer. *Am J Epidemiol.* 2006;163:502.
9. Chow W, Johansen C, Gridley G, et al. Gallstones, cholecystectomy and risk of cancers of the liver, biliary tract and pancreas. *Br J Cancer.* 1999;79:640.
10. Schima W, Ba-Ssalamah A, Kolblinger C, et al. Pancreatic adenocarcinoma. *Eur Radiol.* 2007;17:638–649.

# Safety and Accuracy of Percutaneous Core Needle Biopsy in Examining Pancreatic Neoplasms

***To the Editors:***

Percutaneous imaging-guided fine needle aspiration has been well established

**TABLE 1.** Results of Percutaneous Trucut Biopsies of 124 Pancreatic Masses

| Clinical Diagnosis | Biopsy Pathology | n | Final Diagnosis |
|---|---|---|---|
| Cancer | Adenocarcinoma | 99 | |
| | Adenosquamous carcinoma | 8 | |
| | Undifferentiated cancer | 8 | |
| | Metastatic malignancy* | 2 | |
| | Cancer of uncertain origin | 1 | Pancreatic cancer |
| | Chronic pancreatitis | 1 | Pancreatic cancer |
| Cystadenocarcinoma | Cystadenoma | 5 | Cystadenoma |

*One from gastric cancer with metastasis of celiac lymph nodes and another from extranodal extension of non–Hodgkin lymphoma in the pancreas.

as a useful diagnostic tool for the confirmatory diagnosis of pancreatic malignancies before palliative treatment.[1–5] Percutaneous core needle biopsy (CNB) has been reported not to be superior to fine needle aspiration for the diagnostic accuracy of pancreatic lesions.[5] This study was designed to evaluate the safety and accuracy of percutaneous pancreatic CNB in our hospital.

## MATERIALS AND METHODS

Of 148 patients without prior pancreatic pathologic diagnosis, 124 underwent ultrasound and/or computed tomography (CT)–guided CNB for the pancreatic lesions from December 2003 to May 2010. Twelve patients were with liver metastasis, 26 were with retroperitoneal lymph node metastasis, and 31 were with both. All patients provided written informed consent for the procedure.

Each mass had been evaluated with CT or ultrasound. In addition, platelet count, coagulation profile, serum amylase level, and electrocardiogram were evaluated. Patients fasted from food and water for more than 12 hours, and omeprazole and octreotide were administered before the CNB procedure. An enhanced CT scan within 1 week before biopsy was used as reference to imaging-guided biopsy. The standard procedure for sampling was performed with 16- or 18-gauge Precisa needle (HS Hospital Service SPA, Aprilia, Italy) under ultrasound and/or CT guidance. The insertion site was determined based on the largest diameter and the distinct abnormal echoic area of the mass, as well as the shortest needle track to minimize injury to the patient. Intravenous sedation with propofol was used when patient's intraoperative cooperation was not necessary. When a needle was introduced for the second time, it was thoroughly washed in 75% alcohol, followed by sterile saline. Details regarding CT-guided procedure were similar to those of ultrasound guidance. All samples were fixed in 10% formalin for pathologic evaluation.

Patients fasted from food with monitoring for 4 hours after surgery. Hemostatics, antibiotics, and octreotide were administered according to intraoperative status. Normal diet was gradually restored if no biochemical abnormalities were found.

## RESULTS

The study included 37 women and 87 men (mean age, 57.3 years; range, 28–84 years). The mean size of mass was 3.8 cm (range, 2.6–6.7 cm) in maximum diameter. There were 104 lesions (83.9%) located in the head of pancreas, 18 (14.5%) were located in the body or tail, and 2 (1.6%) involved the entire pancreas. Each procedure yielded a mean of 2.3 strips of tissue (range, 2–5). The stomach and the left lobe of the liver were traversed in 37 and 3 procedures, respectively. Two procedures were passed through the upper pole of the left kidney under CT guidance. Patients were followed up for 1 to 58 months (median, 12.3 months) after the procedure. By histologic examination, the sensitivity, specificity, and accuracy of diagnosis were 99.2%, 100%, and 99.2%, respectively (Table 1).

The procedure was uneventful in 105 (84.7%) of the 124 cases. Three patients had a transient increase in serum amylase (>500 U/L) without clinical symptoms of peritonitis and pancreatitis, which returned to normal after conservative treatment. Five patients experienced worse postprocedural pain without clinically significant findings, and this was relieved within 24 hours. A new subcutaneous mass at the biopsy site was found and confirmed as tumor seeding (pancreatic adenocarcinoma) in 1 patient 134 days after the first biopsy.

## DISCUSSION

Our results showed that 16- or 18-gauge CNB yielded higher diagnostic accuracy. In our experience, it is important for the safety of procedure to minimize the distance from the abdominal wall to the pancreatic lesions by pressing the ultrasound transducer continuously, to keep the biopsy needle as perpendicular as possible to the gastric wall, and to advance the needle forcibly and quickly when penetrating the gastric wall.

A single case with tumor seeding could not be attributed to the biopsy procedure without a doubt because a total of 12 times of punctures had been conducted on the same site for percutaneous cryotherapy and iodine-125 seed implantation during the patient's treatment.

The limitation to our study is that our hospital specializes in mini-invasive treatment of advanced malignancies. Patients treated in our hospital usually had larger tumor with frequent metastases, with more comorbidities, and always had the treatment before admission.

In conclusion, our results demonstrate that ultrasound- or CT-guided percutaneous CNB for pancreatic masses is a safe and simple procedure with optimal diagnostic accuracy for pancreatic neoplasms.

## ACKNOWLEDGMENT

*This work did not receive funding from any organizations. The authors have no potential conflicts of interest.*

**Keqiang Xu, MD**
Department of Digestive Oncology
Fuda Cancer Hospital
Affiliated Fuda Hospital
and Translational Medicine Center
Guangzhou Institutes of Biomedicine
and Health, Chinese Academy of Sciences
Guangzhou, China
xukeqiang@yahoo.com

**Liang Zhou, MD**
Department of Mini-invasive Treatment
Fuda Cancer Hospital
Guangzhou, China

**Bing Liang, MD**
Department of Digestive Oncology
Fuda Cancer Hospital
Guangzhou, China

**Lizhi Niu, MD**
Department of Mini-invasive Treatment
Fuda Cancer Hospital
Affiliated Fuda Hospital
and Translational Medicine Center
Guangzhou Institutes of Biomedicine and Health
Chinese Academy of Sciences
Guangzhou, China

**Xin Zheng, MD**

**Jiongyuan Xu, MD**
Department of Digestive Oncology
Fuda Cancer Hospital
Guangzhou, China

**Daming Yang, MD**
Department of Digestive Oncology
Fuda Cancer Hospital
Affiliated Fuda Hospital
and Translational Medicine Center
Guangzhou Institutes of
Biomedicine and Health
Chinese Academy of Sciences
Guangzhou, China

**Dongfeng Tan, MD**
Department of Pathology
MD Anderson Cancer Center
Houston, TX

**Kecheng Xu, MD**
Fuda Cancer Hospital
Affiliated Fuda Hospital
and Translational Medicine Center
Guangzhou Institutes of
Biomedicine and Health
Chinese Academy of Sciences
Fuda Cancer Hospital
Guangzhou, China

## REFERENCES

1. Carlucci M, Zerbi A, Parolini D, et al. CT-guided pancreatic percutaneous fine-needle biopsy in differential diagnosis between pancreatic cancer and chronic pancreatitis. *HPB Surg*. 1989;1:309–314.
2. Brandt KR, Charboneau JW, Stephens DH, et al. CT- and US-guided biopsy of the pancreas. *Radiology*. 1993;187:99–104.
3. Zamboni GA, D'Onofrio M, Idili A, et al. Ultrasound-guided percutaneous fine-needle aspiration of 545 focal pancreatic lesions. *AJR Am J Roentgenol*. 2009;193:1691–1695.
4. Di Stasi M, Lencioni R, Solmi L, et al. Ultrasound-guided fine needle biopsy of pancreatic masses: results of a multicenter study. *Am J Gastroenterol*. 1998;93:1329–1333.
5. Stewart CJ, Coldewey J, Stewart IS. Comparison of fine needle aspiration cytology and needle core biopsy in the diagnosis of radiologically detected abdominal lesions. *J Clin Pathol*. 2002;55:93–97.

# Morules in Intraductal Papillary Mucinous Neoplasm With an Associated Invasive Carcinoma of the Pancreas

***To the Editor:***

Morules have been considered as a metaplastic lesion, appearing as a mulberry-like, well-circumscribed conglomeration of squamoid cells. Morules have been identified in neoplastic and nonneoplastic lesions of various organs, being particularly well documented in endometrial adenocarcinoma and hyperplasia. However, in the digestive system, they can also occur in gastric polyps, colorectal adenomas and carcinomas, and gallbladder adenomas and carcinomas.[1–3] To date, no published report has documented morules developing in the pancreas. We report morules that were found in a case of intraductal papillary mucinous carcinoma (IPMC) with minimal invasion (intraductal papillary mucinous neoplasm [IPMN] with an associated invasive carcinoma) of the pancreas.

Abdominal computed tomography examination demonstrated a pancreatic tail cyst and dilation of the main pancreatic

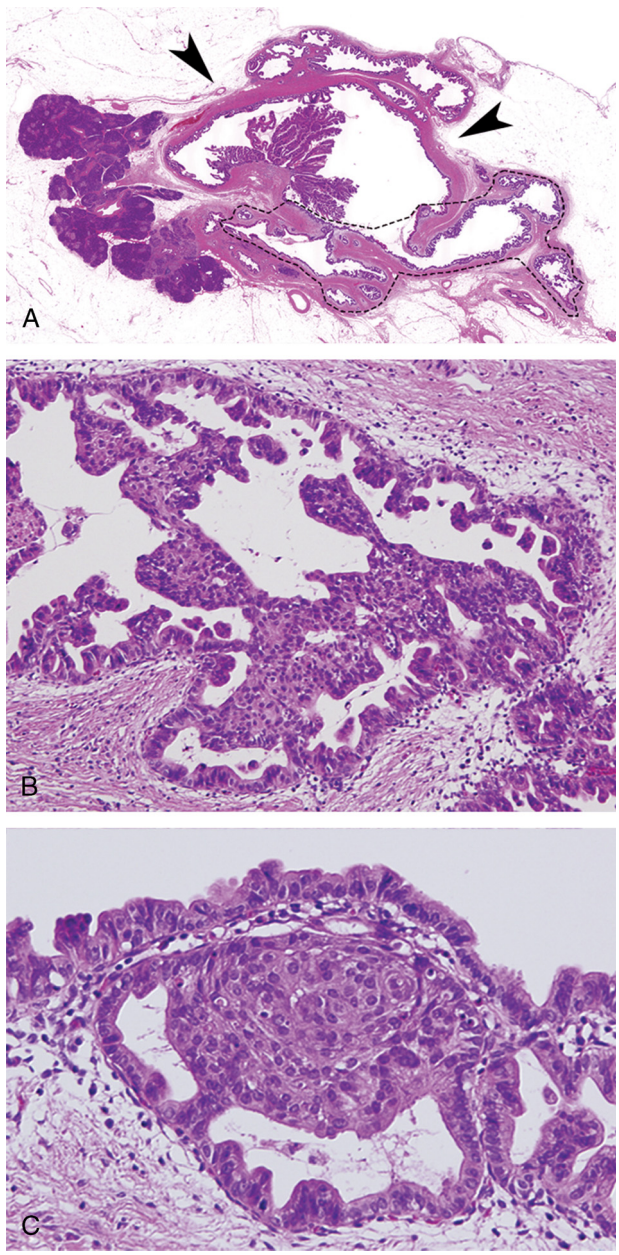


**FIGURE 1.** Histological and immunohistochemical features of the morules in IPMN. A, Morules were formed in the branch duct and main pancreatic duct (arrow head) in the limited area delineated by the dotted line (loupe view). B, Many morules were formed on the luminal side of IPMN cells showing low-papillary features and fused to each other (low-power view). C, The morules were composed of spindle or rounded cells with round nuclei, with neither keratinization nor intercellular bridges (high-power view).