



## Author's reply for letter to editor: Acute pancreatitis-onset carcinoma in situ of the pancreas with focal fat replacement diagnosed using serial pancreatic juice aspiration cytologic examination (SPACE)

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### Answer

Thank you for your valuable comments, and we are glad that you appreciate our paper. We described the contribution of the newly developed diagnostic method “SPACE” in diagnosis of Pancreatic Carcinoma In Situ (PCIS) in the selected patient with acute pancreatitis, pancreatic duct stricture, and fat replacement of pancreatic parenchyma.

PET–CT has the potential to detect pancreatic cancer. It can reveal the tumor size to a certain degree and inflammatory changes with some activity. By EUS, the surrounding fibrosis can be recognized and punctured.

However, PCIS is minute and just exists in the mucosa. Fibrosis is also limited in the pancreas. We presumed that PET–CT cannot reveal PCIS with fibrosis and EUS-FNA does not perform any role in diagnosing PCIS. Thus, we thought that SPACE is the only method to diagnose PCIS in a patient with MPD stricture.

According to our experience, SPACE could contribute to diagnosis of PCIS not only small in size, but also limited to the branch duct. Probably, the potential of SPACE for diagnosing PCIS depends on six serial tests. At present, SPACE is just indicated in patients with abnormality of MPD stricture with or without fat replacement, because some of the abnormalities are associated with PCIS. However, we do not

have information about the other morphological abnormalities induced by PCIS.

Elastography is a new method to characterize pancreatic lesions. The examination reveals the degree of stiffness of the lesion mainly due to fibrosis. It could contribute to selecting cases for SPACE because PCIS induces fibrogenesis around the lesion. However, elastography has a low sensitivity and a low specificity for indicating the stiffness.

PCIS may not progress to an advanced and usual case of pancreatic cancer, as it has the tendency to spread wide along the pancreatic duct without destroying the basement membrane. However, PCIS diagnosed by SPACE has the characteristic of fibrosis in the surrounding tissue, which could suggest PCIS interaction with the parenchyma and favorable circumstances for invasion. Moreover, as we came across more number of cases, we realized that some cases with wide spread PCIS have a point of destruction of the basement membrane due to invasion.

Commonly, pancreatic cancers are highly advanced and have a large diameter. The surrounding tissues are destroyed by the tumor, and early stage findings might be lost. Whether widespread PCIS is the initial change cannot be revealed. However, some cases with advanced cancer are accompanied with widely spread PCIS around the tumor. Maybe, cancer cells lead the change of neighborhood cells from normal to cancerous and expand gradually acquiring the characteristic of invasiveness by interaction with the surrounding tissue.

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