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Experience with the new SonoTip TopGain® FNB needle

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Introduction

EUS guided fine needle aspiration (EUS-FNA) was developed in the early 1990s by our group in collaboration with MediGlobe (1, 2). During this pioneering era, indications of EUS guided FNA sampling were defined and include at present the staging of upper gastrointestinal and lung cancer, as well as primary diagnosis of lymph nodes, submucosal tumors, adrenals, pancreas and the biliary tract (3, 4). Today, EUS-FNA is widely accepted and the cornerstone of the diagnostic process both in gastroenterology as well as in pulmonology, the latter when combined with endobronchial ultrasound guided transbronchial needle aspiration biopsy (EBUS-TBNA). However, our clinical experience during nearly 30 years have demonstrated that EUS guided fine needle aspiration with cytological evaluation has some limitations at least for some specific diseases as well as in situations where subclassification of different lesions are needed and where single cells or clusters of cells do not suffice but where preserved tissue architecture is important.

Recently, new needle designs have been developed for EUS guided biopsy with the aim to harvest more tissue for histology, challenging conventional aspiration needles.

The aim of this report is to share our experience with the new SonoTip TopGain® FNB needle and to present examples where the bioptic results obviously showed important histological information not seen by cytology.

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What is the general advantage of using FNB needles compared to FNA needles?

It is at present evident the advantage of using FNB needles is that fewer passes per lesion is needed to obtain a diagnosis compared to FNA needles. According to the literature, 2 passes are sufficient for a diagnosis of pancreatic lesions compared to 3 passes with FNA (5). In addition to this it is also documented that the type of FNB needle matters. In this respect crown cut needles are preferred over side-beveled needles (6) (Figure 1). Furthermore, the main advantage of a crown cut needle compared to a standard cut FNA needle is its ability to harvest bigger specimens where the tissue architecture is preserved (6).

Figure 1

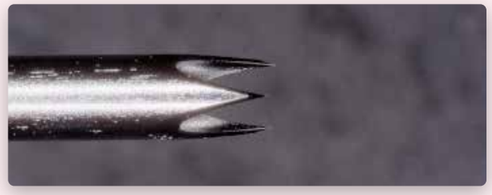


Photo showing a crown cut needle (Franseen needle type)

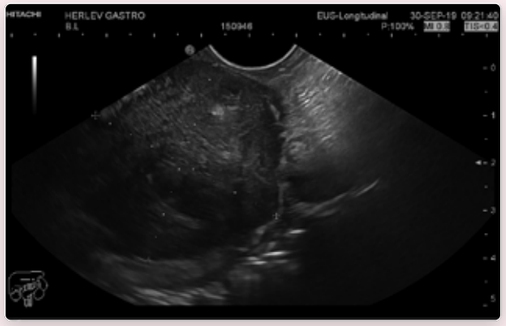
When should the SonoTip TopGain FNB needle be preferred over the standard FNA needle?

The question is then when is it advisable to use the SonoTip TopGain FNB needle instead of a standard SonoTip ProControl FNA needle? There is no doubt that in many situations the standard FNA needle is sufficient and will be for some time. The clinical question is most often whether a lesion is cancer or not! For this, cytology is sufficient since this question can be evaluated simply by evaluating the morphology of the cells and nuclei. However, more and more clinical questions are no longer limited to the question of cancer/no cancer. Immunohistochemical analysis is often used to either differentiate between two separate tumor types or to subclassify specific lesions (ie lymphomas, neuroendocrine tumors, submucosal lesions) and for this histology is preferable. In addition, molecular analysis has become increasingly important for therapeutic decisions in oncology and therefore histology is also more qualified and preferred over cytology (7). In the early era of personalized medicine the interest in growing organoids from cancers is increasing and within a few years oncological therapies will rely on individualized reactions from testing various chemotherapeutic agents of these cell cultures (8) (Figure 2).

Figure 2

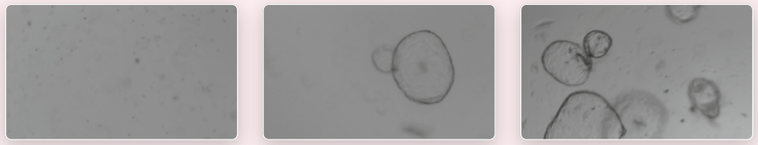
A 74-year old lady referred for EUS showing a hypervascular tumor in the head of the pancreas, no activity on PET.

- **EUS suggested diagnosis:** suspicious for NET. EUS-FNB was performed with 3 passes
- **Pathology FNB diagnosis:** inconclusive, insufficient tissue
- One EUS-FNB sample was purified and seeded as organoid culture

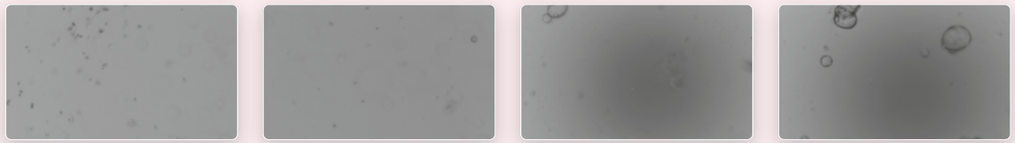


Organoid cultures clearly showing viable cells from the EUS-FNB samples

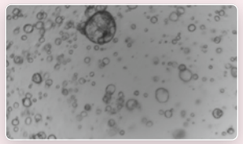
Passage 0



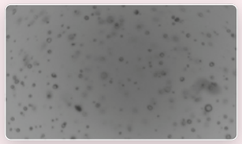
Passage 1



Passage 2

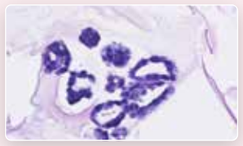


Passage 3



Following 3 passages, the organoids were harvested and a formalin fixed paraffin embedded block was produced

H&E



CK7

MUC5AC

Immune staining of the cells were negative for IMP3, s100P, pVHL. This is not indicative for a pancreatic ductal adenocarcinoma (PDAC)!

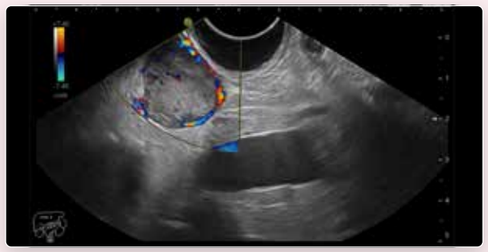
In the meantime the patient underwent surgical resection (Whipple) due to the suspicion of PDAC Diagnosis of the surgical specimen: solid serous adenoma, panIN foci in close proximity. Unfortunately, the patient died from complications of the Whipple procedure (leakage).

A mutational analysis on organoids and the surgical specimen post mortem demonstrated both a deletion of the VHL gene (linked to serous adenoma), explaining the negative immune staining of pVHL) pointing towards serous adenoma and not PDAC. Would these results from the EUS-FNB organoid culture have prevented the decision to resect?

An example of a case study where EUS-FNB with culturing of organoids and molecular testing may become an important possibility of improving diagnosis and stratifying oncological therapy.

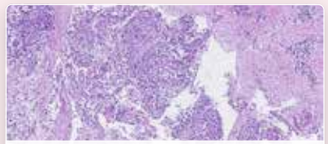
At present it is suggested to use the SonoTip TopGain needle in cases where the clinical question requires a differentiation of a lesion between two tumor types, for instance whether a suspicious lymph node either in the mediastinum or abdomen is a metastasis from a renal cancer, a colon cancer, a breast cancer or a gynecological cancer of which the patient was treated for earlier. Also, for the diagnosis of submucosal lesions the FNB needle should be preferred (Figure 3).

Figure 3



EUS guided FNB from a submucosal lesion in the duodenum. Histological analysis shows an overview of a well preserved specimen first, secondly an enlarged image demonstrating spindle cells. A final immunostaining with CD 117 shows significant staining confirming the diagnosis of a Gastrointestinal stomal tumour (GIST).

Preserved specimen



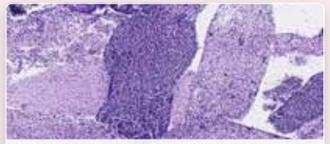
Spindle cells

Immunostaining with CD 117

In the diagnosis of GIST tumors it is documented that FNB needles are more sensitive than FNA needles and evaluation of the histological specimen is often the cornerstone in the diagnosis and therapeutic management of these patients (9). The diagnosis of lymphomas may sometimes be difficult and for this the differentiation of the subtype requires enough tissue where cytology is insufficient (Figure 4).

Figure 4

Tissue fragments



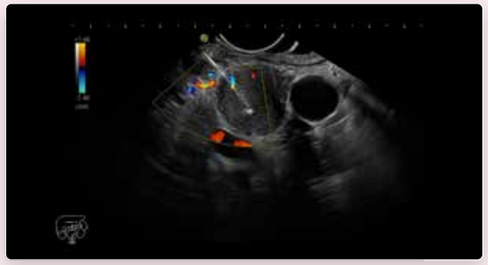
Numerous immature B lymphocytes

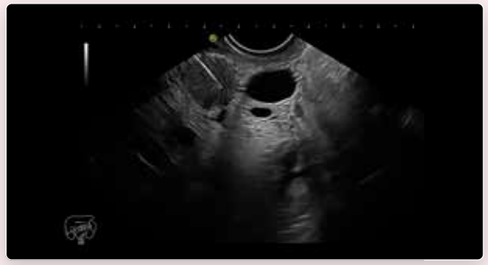
Immune colouring with PAX5

Histological images obtained with EUS-FNB with the TopGain 22 G needle shows first an overview demonstrating well preserved tissue fragments, secondly an enlarged image demonstrating numerous small immature B lymphocytes. The final image of the specimen with immune colouring with PAX5 confirms a diagnosis of small cell lymphocytic B cell lymphoma (SCLL).

If the clinical question may be to differentiate between a sarcoid lesion and a lymphoma or an adenocarcinoma metastases and a lymphoma, the SonoTip TopGain FNB needle is the needle of preference (10). There are a range of other clinical situations where an FNB needle should be used. This can be diagnosis of neuroendocrine tumors of the pancreas (Figure 5).

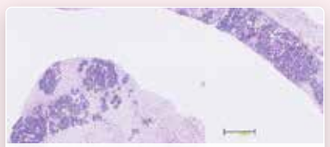
Figure 5





2 images showing the EUS guided FNB with the TopGain needle. The tumor is located in the head of the pancreas and is obviously well vascularized and hard to puncture. The photos show first the wellpreserved specimen (HE stained) in overview, secondly an enlarged view demonstrating neuroendocrine cells. Finally, immunostaining confirmed the diagnosis of a NET with low malignant potential by immunostaining with Chromogranin A.

HE stained specimen



Neuroendocrine cells

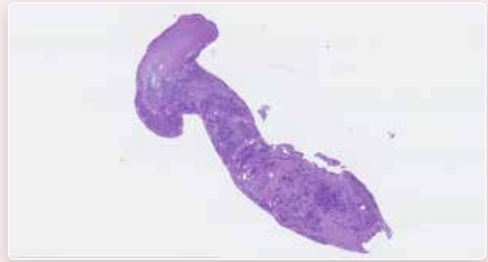
Immunostaining

Often the differential diagnosis of such a lesion is difficult based on EUS alone since it often resembles a primary adenocarcinoma. Due to this diagnostic dilemma and since genetic analysis is increasingly requested for therapeutic decisions in patients with pancreatic cancer, we often use the SonoTip TopGain FNB needle as our standard needle for the diagnosis and classification of a pancreatic neoplasm. Finally, although a rare entity among the EUS cohort of patients, the diagnosis of sarcomas should be mentioned. This tumor type is also best diagnosed by histology (11).

Clinical results with the Sono Tip TopGain FNB needle

Based on our experience with EUS guided biopsy using the SonoTip TopGain FNB needle, our pathologists are very pleased about the size of the tissue fragment and about how well preserved the specimen is (Figure 6).

Figure 6



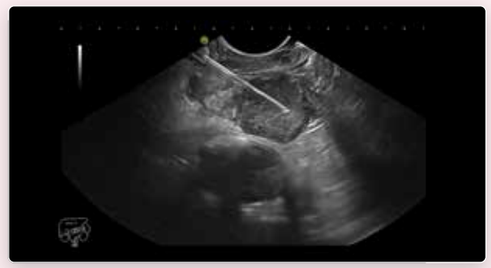
An example of a well preserved histological specimen obtained by EUS-FNB with the 22 G SonoTip TopGain Needle

We have tested both, 22 and 25 Gauge SonoTip TopGain FNB needles in a variety of different lesions. Our results show that the size of the specimens differs significantly between the 22 G needle and the 25 G needle where the 22 G needle harvests the biggest specimen. This is also the case when we compare the TopGain FNB needles with traditional FNA needles of comparable size, ie the TopGain FNB needle obtains obviously the largest samples.

The penetration force needed to penetrate hard lesions during the EUS guided biopsy procedure seems slightly higher compared to standard FNA needles, and in a few cases a stabbing technique have to be used in order to compensate for the resistance from the lesion.

Needle visualization during the biopsy procedure is very good and comparable to a similar size standard SonoTip ProControl FNA needle (Figure 7).

Figure 7



EUS-FNB of a 2 cm ecco-poor lesion between the head of the pancreas and the duodenum demonstrating the needle visibility.

Conclusions

Nearly 30 years have passed since the first EUS guided fine needle aspiration was performed, but fine needle cytology cannot stand alone in modern gastroenterology and pulmonology. Increasingly, todays clinical questions rely on sufficient material as well as preserved tissue architecture obtained from lesions outlined by endosonography. The SonoTip TopGain FNB needle is a true 3rd generation needle for EUS guided diagnosis and subclassification of a variety of lesions and this needle type should be part of a fully equipped diagnostic armamentarium for EUS guided diagnostics.

Summary

Suggestions for use of the SonoTip TopGain FNB needle:

- Differentiation between 2 different neoplasms
- Submucosal lesions
- Lymphomas
- Neuroendocrine tumors
- Sarcoidosis
- Sarcomas
- If more cellular material is needed for molecular analysis (pancreatic cancer, lung cancer)
- If good material for immunohistochemical analysis is warranted

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