

# Rapid on-site cytologic evaluation during endoscopic ultrasound-guided biopsies of pancreatic solid lesions

## *Evaluación citológica en sala durante las biopsias de lesiones pancreáticas sólidas guiadas por ultrasonido endoscópico*

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### Abstract

**Background:** Endoscopic ultrasound-guided fine-needle biopsy (EUS-FNB) is safe and effective for the diagnosis of pancreatic adenocarcinoma. Although rapid on-site evaluation (ROSE) can improve tissue collection and increase diagnostic yield, its utility has been recently questioned. **Objective:** Determine the diagnostic efficacy of EUS-FNB with ROSE of pancreatic masses in a new echoendoscopy unit. **Methods:** Cross-sectional and comparative study of patients who underwent EUS-FNB of pancreatic masses between January and July 2017. Patient demographics, ultrasonographic details, and pathology reports were examined. **Results:** A total of 23 procedures were analyzed. Median age was 59 years (range: 46-77). The group with ROSE had 13 patients (56.5%) and the group without ROSE 10 (43.5%). The final pathology report showed enough and adequate sample in 100% of the group with ROSE (13/13 vs. 5/10;  $p = 0.007$ ). Diagnosis of malignancy was established in 84.6% of the biopsies (11/13 vs. 2/10;  $p = 0.003$ ) in the group with ROSE. **Conclusions:** ROSE is useful to improve the diagnostic efficacy of EUS-FNB of pancreatic masses, especially in new EUS centers or in centers with a low diagnostic yield.

**Keywords:** Endoscopic ultrasound. Pancreatic neoplasms. Fine-needle biopsy. Rapid on-site cytopathologic evaluation.

### Resumen

**Antecedentes:** La biopsia con aguja fina guiada por ultrasonido endoscópico (BAF-USE) es segura y eficaz para el diagnóstico del adenocarcinoma pancreático. La revisión citológica rápida en sala (ROSE, rapid on-site evaluation) puede mejorar la calidad de la muestra y el rendimiento diagnóstico; en años recientes se ha cuestionado su utilidad. **Objetivo:** Determinar la eficacia diagnóstica de la ROSE durante las BAF-USE de lesiones pancreáticas sólidas en un nuevo centro de ecoendoscopia. **Métodos:** Estudio transversal y comparativo en el que se incluyeron todos los pacientes a quienes se realizó BAF-USE de lesiones pancreáticas sólidas entre enero y julio de 2017. Se evaluaron datos demográficos, ecográficos y de patología de las BAF-USE. **Resultados:** Se analizaron 23 procedimientos. La mediana de edad fue de 59 años (rango: 46-77). En el grupo

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con ROSE hubo 13 pacientes (56.5%) y en el grupo sin ROSE hubo 10 (43.5%). En el grupo con ROSE, el reporte de patología mostró muestra adecuada en el 100% (13/13 vs. 5/10;  $p = 0.007$ ), así como diagnóstico de malignidad en el 84.6% (11/13 vs. 2/10;  $p = 0.003$ ). **Conclusiones:** La ROSE es una herramienta útil para mejorar el diagnóstico de BAF-USE de lesiones pancreáticas sólidas, principalmente cuando hay bajo rendimiento diagnóstico y en nuevas unidades de ecoendoscopia.

**Palabras Clave:** Ultrasonido endoscópico. Neoplasias sólidas del páncreas. Biopsia con aguja fina. Revisión citológica en sala.

## Introducción

Pancreatic cancer is the seventh leading cause of cancer death in the world. Five-year survival is lower than 9%<sup>1</sup>. Approximately 20% are estimated to be resectable with potentially curative purposes<sup>2</sup>. Therefore, early diagnosis is crucial to offer the patient an appropriate treatment and improve his prognosis.

Since its introduction in 1992, endoscopic ultrasound-guided fine-needle biopsy (EUS-FNB, with or without aspiration) has become an indispensable tool in the study of lesions adjacent to the gastrointestinal tract, as well as in the study of sub-epithelial gastrointestinal lesions<sup>3</sup>. It is a safe, minimally invasive, effective, and highly accurate technique, especially for solid lesions of the pancreas<sup>4-7</sup>. Complications associated with this procedure are low and are generally reported in 0-2% of cases<sup>8,9</sup>. Its most important limitation is that the cytological specimen may have poor cellularity and lack of histological architecture<sup>4</sup>.

Rapid on-site evaluation (ROSE) consists of immediate evaluation of samples obtained by EUS-FNB, in terms of sufficiency and preliminary diagnosis<sup>10,11</sup>. At present, the evidence is controversial, since EUS-FNB has been established as a technique with high diagnostic yield (85-87%), high sensitivity (94-96%), and high specificity (95-100%), even without the addition of ROSE<sup>3,6,7,12</sup>. Furthermore, the so-called second-generation histological needles have shown promising results in terms of sufficiency, cellular structure, and diagnostic yield<sup>13,14</sup>.

Achieving high diagnostic yield requires overcoming multiple limiting steps, mainly experience of the endosonography, characteristics of the needle, tissue acquisition technique, and experience of the pathologist<sup>15</sup>. Therefore, the availability of ROSE might improve sample-taking by EUS-FNB of pancreatic solid lesions in centers where endoscopic ultrasound is starting to be introduced, in those where there are physicians in training and in those with low volume. The purpose of this study was to compare the diagnostic efficacy of

ROSE during EUS-FNB of solid pancreatic lesions as part of the initial experience at a national reference center in Mexico.

## Methods

A retrolective, comparative study was carried out. All patients of both genders, older than 18 years, with EUS-FNB indication for presenting with solid lesions of the pancreas, in the period from January to July 2017, who were cared for by the endoscopy department of the National Medical Center *20 de Noviembre*, were included in the study. The study was approved by the institutional ethics committee, and all patients granted written informed consent prior to the procedure. Biopsies were taken by two endosonographers, and sedation was assisted by the anesthesiology department.

The biopsy results were divided in two groups: a group with ROSE, in which cytological examination was carried out at the endoscopy room until the sample was considered adequate and subsequently was sent to the pathology department for definitive analysis, and another group without ROSE, in which the biopsies were preserved in 10% formalin and sent to the pathology department.

## Technique

The EUS-FNBs were taken with a 22-G needle, without aspiration, with a stylet and slow withdrawal; at least two passes were required with five entries in four directions using a fan technique (Figs. 1 and 2). An EG-530UT linear ultrasound endoscope coupled to a SU-8000 console (Fujifilm Corporation, Minato-Ku, Tokyo, Japan) was used.

## Definitions

- Adequate sample: when the pathologist analyzed the sample and confirmed the presence of

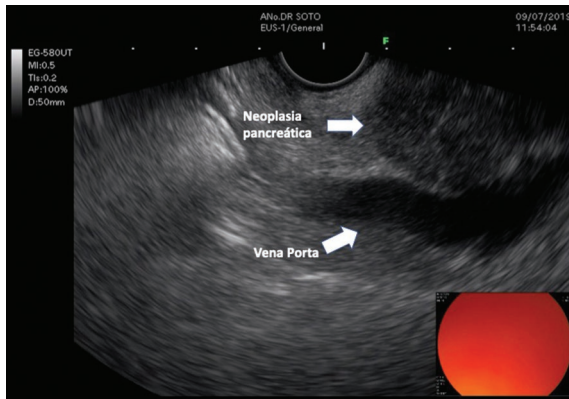


**Figure 1.** Pancreatic adenocarcinoma endoscopic ultrasound image. *Neoplasia pancreática*: pancreatic neoplasm; *Vena porta*: portal vein.

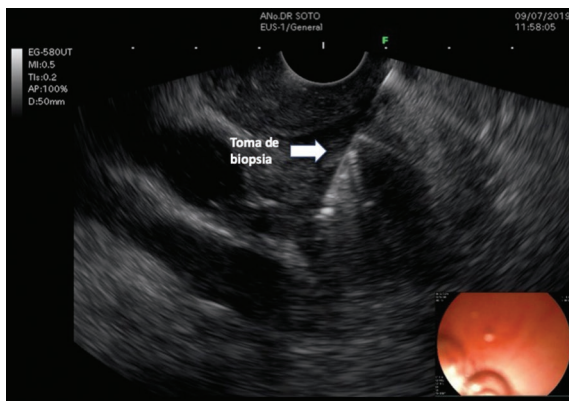


**Figure 2.** Pancreatic adenocarcinoma fine needle biopsy endoscopic ultrasound image. *Toma de biopsia*: biopsy take.

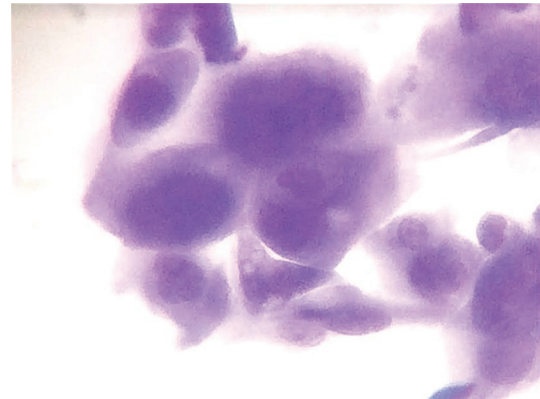


**Figure 3.** Representative image of the cytopathological examination in the room (staining with toluidine blue).

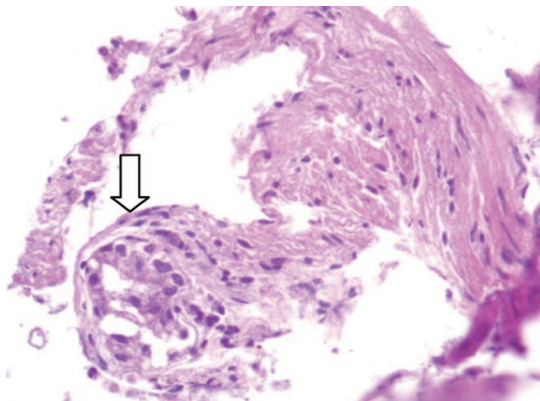


**Figure 4.** Moderately-differentiated ductal adenocarcinoma obtained by endoscopic ultrasound-guided fine needle biopsy (cell block, staining with hematoxylin and eosin).

sufficient glandular or ductal cells to establish histopathological diagnosis. In the group with ROSE, if the sample analyzed at the endoscopy room was not adequate, another pass was made until confirming that the sample was adequate (Figs. 3 and 4).

- Inadequate sample: it was defined when there was acellularity, necrosis, absence of glandular or ductal cells, or insufficient material for diagnosis, and when it was literally reported as inadequate.
- Final diagnosis: when definitive report was provided by the pathology department to rule out or confirm the presence of atypia or malignancy.

### Statistical analysis

To evaluate the results, descriptive statistics were used with frequencies, percentages, medians and

ranges. Differences between groups were analyzed using the chi-square test or Fisher's exact test for categorical variables and Student's t-test or Mann-Whitney's U-test for continuous variables, as appropriate. Statistical analysis was performed with SPSS (version 21, IBM Corp., Armonk, New York, USA).

### Results

Twenty-three patients were included, median age was 59 years (range: 46-77) and 12 (52.2%) were females. In ten patients (43.5%), EUS-FNB was performed without evaluation in the endoscopy room (group without ROSE), and in 13 patients (56.5%), a rapid cytological evaluation was carried out in the room (ROSE group). Table 1 shows the population main characteristics, as well as pancreatic lesions location and size.

**Table 1. General characteristics of the study population**

|                       | Group with ROSE (n = 13) (% or range) | Group without ROSE (n = 10) (% or range) | p    |
|-----------------------|---------------------------------------|------------------------------------------|------|
| Age, years            | 60 (47-77)                            | 58 (46-72)                               | 0.39 |
| Female gender         | 6 (46.2)                              | 6 (60)                                   | 0.68 |
| Lesion location       |                                       |                                          | 0.87 |
| Head of pancreas      | 8 (61)                                | 7 (70)                                   |      |
| Uncinate process      | 3 (23.1)                              | 1 (10)                                   |      |
| Body of pancreas      | 1 (7.7)                               | 1 (10)                                   |      |
| Tail of pancreas      | 1 (7.7)                               | 1 (10)                                   |      |
| Lesion size           |                                       |                                          | 0.22 |
| <30 mm                | 8 (61.5)                              | 3 (30)                                   |      |
| ≥30 mm                | 5 (38.5)                              | 7 (70)                                   |      |
| Passes during EUS-FNB | 2 (2-3)                               | 3 (3-4)                                  | 0.21 |

EUS-FNB: endoscopic ultrasound-guided fine needle biopsy; ROSE: rapid on-site evaluation.

**Table 2. Histological diagnosis of the lesions in all studied patients**

| Type of lesion                | Absolute frequency (n) | Relative frequency (%) |
|-------------------------------|------------------------|------------------------|
| Pancreatic adenocarcinoma     | 8                      | 34.8                   |
| Cellular atypia, inconclusive | 5                      | 21.7                   |
| Neuroendocrine tumor          | 3                      | 13.1                   |
| Benign lesions                | 2                      | 8.7                    |
| Insufficient material         | 5                      | 21.7                   |
| Total                         | 23                     | 100                    |

**Table 3. Sample considered adequate and definitive diagnosis on histopathology final report**

|                                | Group with ROSE<br>(n = 13)<br>(56.5%) (%) | Group without ROSE<br>(n = 10)<br>(43.5%) (%) | p     |
|--------------------------------|--------------------------------------------|-----------------------------------------------|-------|
| Adequate and sufficient sample | 13 (100)                                   | 5 (50)                                        | 0.007 |
| Malignancy diagnosis           | 11 (84)                                    | 2 (20)                                        | 0.003 |

ROSE: rapid on-site evaluation.

The cytology diagnoses for the 23 lesions studied based on EUS-FNB are detailed in table 2. In the group without ROSE, five samples (50%) were inadequate, while in the ROSE group, all 13 samples (100%) were adequate, with a significant difference ( $p = 0.007$ ). The number of passes was lower in the ROSE group, with no significant differences when compared with the group without ROSE (2 vs. 3;

$p = 0.21$ ). In the group without ROSE, only one patient (10%) had a diagnosis of malignancy, in comparison with ten patients (76.9%) in the group with ROSE ( $p = 0.003$ ) (Table 3).

EUS-FNB diagnostic rate in the group without ROSE was 20%, in comparison with 84.6% in the group with ROSE ( $p = 0.003$ ).

## Discussion

EUS is the most useful technique for pancreatic cancer diagnosis<sup>16</sup>, with a global yield higher than 83%<sup>3,7,17</sup>. In Mexico, there are still few hospitals that have this tool. In our center, it is available since 2015, which has been a real challenge, since creating a reference center has required the training of staff, dissemination of its usefulness and support of the departments that are involved. When analyzing our results, we found a large number of cytology evaluations reported as negative or without sufficient sample. This was the driving force for inviting pathologists to evaluate some cases in our endoscopy room.

ROSE has been shown to be useful in multiple studies<sup>11</sup>. In the meta-analysis carried out by Hébert-Magee et al.<sup>18</sup>, 34 studies with a total of 3644 patients were included in the study, and an overall sensitivity of 88.6% for the diagnosis of pancreatic adenocarcinoma was found, with a specificity of 99.3%. ROSE remained a determinant of EUS-FNB diagnostic yield. On the other hand, in the meta-analysis and systematic review carried out by Kong et al.<sup>19</sup>, 1299 patients were evaluated and no differences were found when ROSE was added to the

evaluation of pancreatic and lymph node biopsies. These evidence controversies make it difficult to know ROSE current role, which is why some experts consider it a “useful and desirable luxury”<sup>2</sup>, although not indispensable. In addition, second-generation histological cutting needles have recently been incorporated. These needles were not used in the present study, but it is worth mentioning the meta-analysis carried out by the group of Todd Baron et al.<sup>13</sup>, in which the usefulness of traditional needles was compared with second-generation histological needles, in scenarios with and without ROSE. The authors concluded that using second-generation histological needles is comparable to using a traditional needle and having ROSE<sup>13</sup>. With these contradictions in evidence, it is difficult to know the real usefulness of ROSE, since this reflects the complexity of a procedure in which success depends on factors related to the endoscopist, the type of needle, the technique used, the number of passes, processing of the sample and experience of the pathologist or cytology technician<sup>3,20,21</sup>.

In our initial experience, the use of ROSE resulted in a larger number of suitable samples, higher diagnostic yield and a higher number of malignancy definitive diagnoses (Tables 2 and 3). One of the limitations of our study was the sample size; however, it is a center that has recently incorporated endoscopic ultrasound, and thus we believe that this may represent the reality of many centers that seek adding this technology to their endoscopy units. We also believe that having invited the pathology department to the endoscopy room was an important step toward improving multidisciplinary participation more directly in the approach of patients with solid pancreatic lesions. This change impacted the way they evaluate these cases, since it makes them understand the great effort it takes to obtain these samples. This is the real importance we found in our work: to expose our experience to other centers where endoscopic ultrasound biopsy diagnostic rate is still low.

## Conclusions

ROSE in EUS-FNB improves diagnostic yield in pancreatic solid lesions. We consider that it is a useful tool in centers with low diagnostic yield.

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## Conflict of interests

The authors declare that they have no conflicts of interests relevant to the performance of this work.

## Ethical disclosures

**Protection of human and animal subjects.** The authors declare that no experiments have been performed on humans or animals for this research.

**Confidentiality of data.** The authors declare that they have followed the protocols of their work center on the publication of patient data.

**Right to privacy and informed consent.** The authors have obtained informed consent from the patients and/or subjects referred to in the article. This document is in the possession of the corresponding author.

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