

# Macroscopic On-site Quality Evaluation (MOSE) Of Biopsy Specimens To Improve The Diagnostic Accuracy During EUS-guided FNA Using A 19-gauge Needle For Solid Lesions: A Multicentre Prospective Randomized Controlled Study



**CHONG, Charing Ching-ning**  
Department of Surgery, Prince of Wales Hospital  
The Chinese University of Hong Kong  
Hong Kong SAR

# Background

- EUS-FNA : Indispensable tool for tissue acquisition
- Outcomes of EUS-FNA results vary
- Specimen inadequacy for pathological evaluation is one of the major factors
- Various methods to improve the diagnostic yield of EUS-FNA:
  - Different size and shape of the FNA needles
  - Different puncture techniques during FNA

# On-site cytopathologist

- Presence of on-site cytopathologist improves diagnostic sensitivity
- If no cytopathologist is present, need more passes

**Table 4.** Select Studies Evaluating the Role of Onsite Cytopathology Service at EUS-Guided FNA

Study	Patients, n	Diagnostic yield, OP vs no OP	Indeterminate samples, OP vs no OP	Unsatisfactory, OP vs no OP
Klapman et al <sup>19</sup>	195	78% vs 32%, $P = .001$	10% vs 12%, $P = .9$	9% vs 20%, $P = .003$
Iglesias-Garcia et al <sup>22</sup>	182	97% vs 86%, $P = .01$	2.1% vs 10.3%, $P = .02$	1% vs 13%, $P = .002$
Alsohaibani et al <sup>23</sup>	104	77% vs 53%, $P = .01$	23% vs 47%, $P = .001$	0% vs 17%, $P = \text{NS}$

OP, onsite pathology; NS, not significant.

*Varadarajulu et al. Clin Gastro Hepatol 2012*

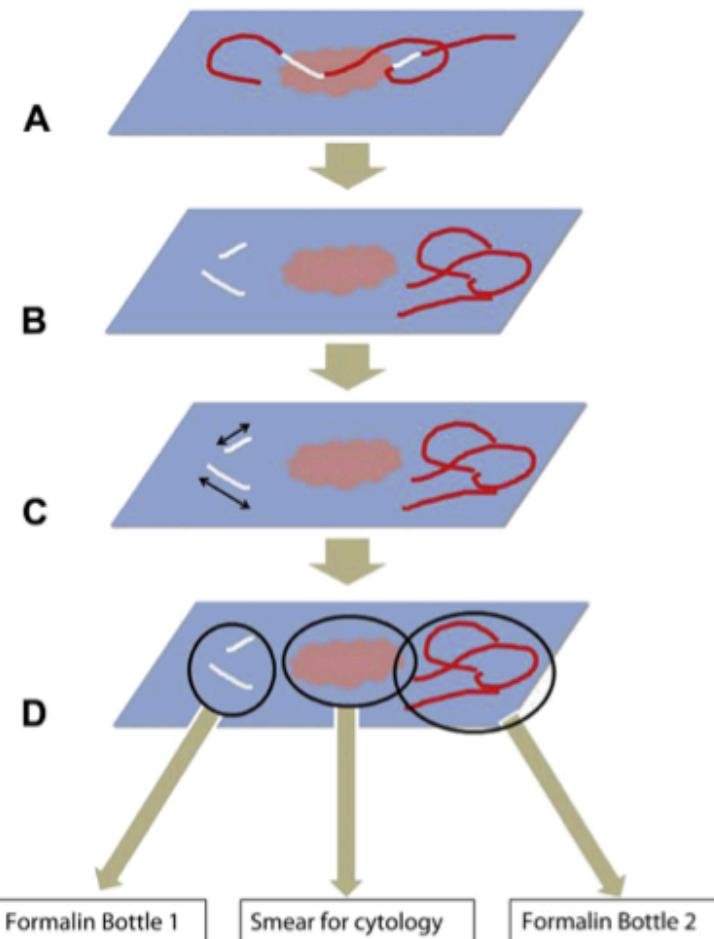
**In many Asian endoscopy centers, on-site cytopathologist is not available because of limited financial and human resources**

# Macroscopic on-site quality evaluation of biopsy specimens to improve the diagnostic accuracy during EUS-guided FNA using a 19-gauge needle for solid lesions: a single-center prospective pilot study (MOSE study)

Takuji Iwashita, MD, PhD,<sup>1</sup> Ichiro Yasuda, MD, PhD,<sup>3</sup> Tsuyoshi Nakashima, MD, PhD,<sup>1</sup> Shinya Uemura, MD, PhD, Masahito Shimizu, MD, PhD,<sup>1</sup> Yuichiro Hatano, MD,<sup>2</sup> Akira

Gifu, Kanagawa, Japan

The aim of this study is to evaluate the quantity and quality tissue obtained and the diagnostic ability of MOSE when compared with the conventional combined histologic-cytologic analysis



# Methodology

## Study design

- Multicentre prospective randomized comparative study



EUS group members

## Setting

- University teaching hospitals and Asian EUS group members

# Requirements for centres participating in the study



1. Provision of certificate of approval from the institute's IRB within 6 months.
2. Provision of an on-site co-investigator who would be responsible for conduction of the study and maintenance of the quality of data.
3. The dedicated site co-investigator have to attend pre-trial investigator meeting which would be held during APDW in Taiwan or International endoscopy workshop in Dec in Hong Kong
4. Have a designated cytopathologist to perform all cytopathologic examination and report in the format as per protocol
5. Centers have to cover the local study expenses

Participating Centers	Country	Site PI
Prince of Wales Hospital	Hong Kong	Charing Chong
Gifu University Hospital	Japan	Takuji Iwashita
University of Malaya Medical Centre, University of Malaya	Malaysia	Chan Wah Kheong
National University Hospital, Singapore	Singapore	Low How Cheng
Beijing Union Medical College Hospital	China	Yang Aiming
Aichi Cancer Center Hospital	Japan	Kazuo Hara
King Khalid University Hospital, King Saud University	Saudi Arabia	Majid A Almadi
Teikyo University Mizonokuchi Hospital	Japan	Ichiro Yasuda
Asian Institute of Gastroenterology	India	Sundeep Lakhtakia
Siriraj Hospital	Thailand	Nonthalee Pausawasdi
Kitasato University Hospital	Japan	Mitsuhiro Kida
Tokyo Medical University	Japan	Takao itoi
Changi General Hospital	Singapore	Ang Tiing Leong
National Taiwan University Hospital	Taiwan	TY Cheng
Medanta, the Medicity, Gurgaon	India	Rajesh Puri
Changhai Hospital, Second Military Medical University	China	Can XU

# Methodology

## Inclusion criteria

- Consecutive patients
- Aged between 18 and 80 years
- Referred for EUS-guided tissue acquisition for evaluating intestinal or extra-intestinal solid lesions with 19G needle
- More than 2cm in the largest diameter

## Exclusion criteria

- Coagulopathy
- Previous history of upper gastrointestinal surgery
- Contraindications for conscious sedation
- Pregnancy
- Informed consent not available

# Methodology

## Randomization

- Randomized in the endoscopy centre via study website
- 1:1 basis
- MOSE vs the conventional technique
- The patients and the pathologists will be blinded to the type of EUS-FNA technique.

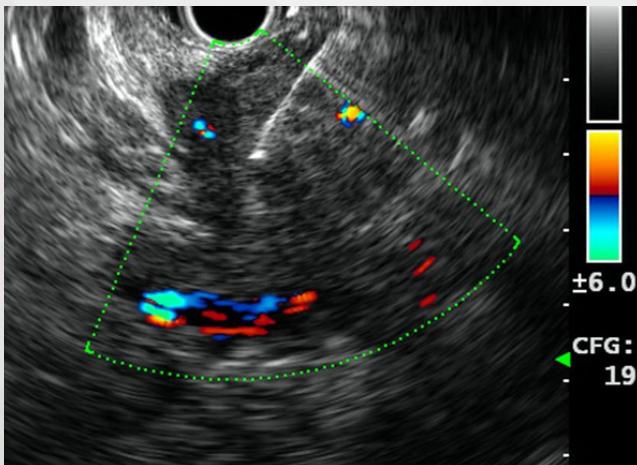
## Standardization of techniques

- Participating investigators will attend a pre-trial training course of MOSE

# Procedures

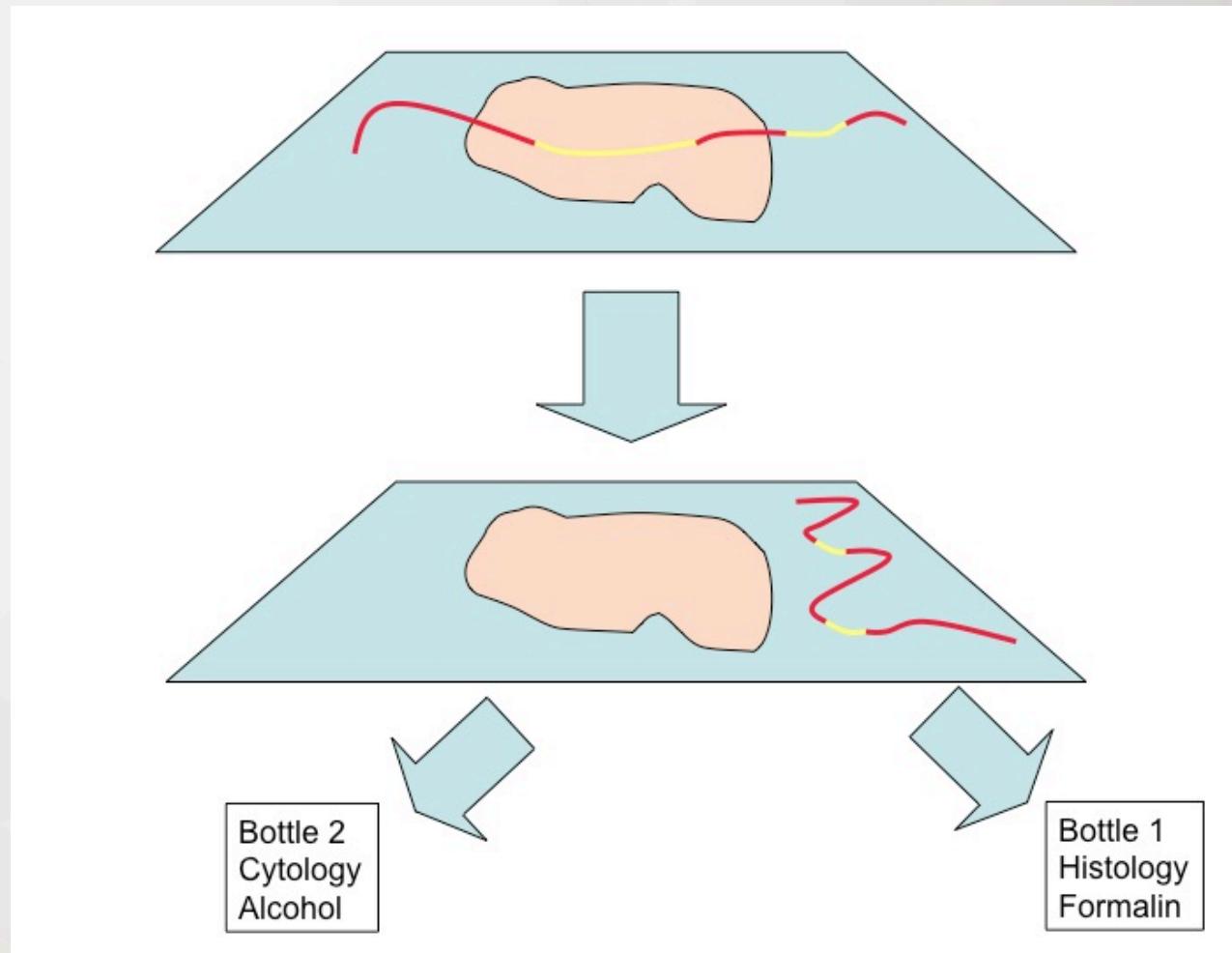
In both arms:

- Conscious sedation
- Examination of the lesion with linear scope
- Puncture with a 19G needle
- No stylet
- 10cc suction
- On site cytopathologic assessment is not available in any of the cases



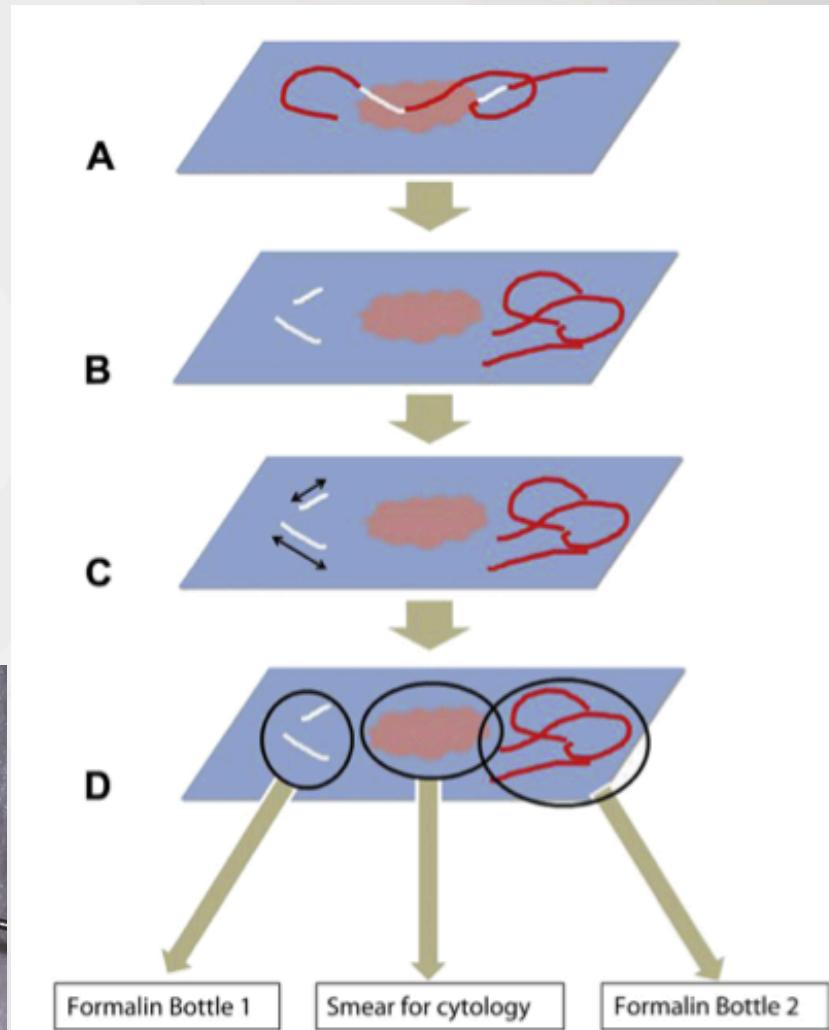
# Procedures - Control arm

- At least 3 passes
- To and fro at least 3 – 5 times
- Solid or paste-like material would be sent in a separate formalin bottle for histology
- Liquid material will be fixed in alcohol and sent for cytological analysis.



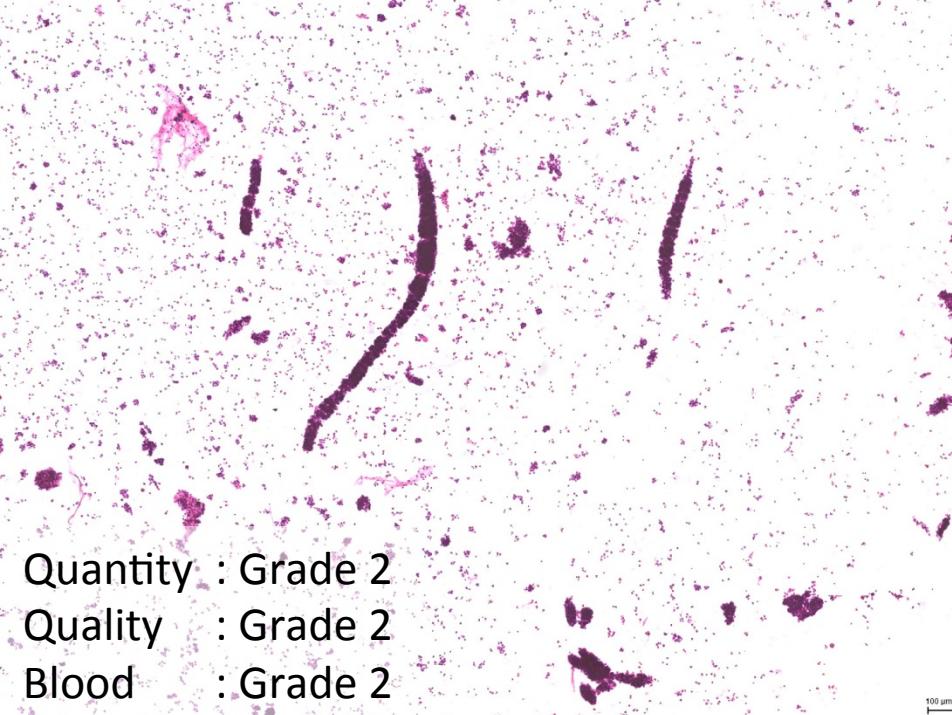
# Procedures - MOSE arm

- The total length of the MVC is measured
- EUS-FNA is completed once the MVC obtained is >4mm

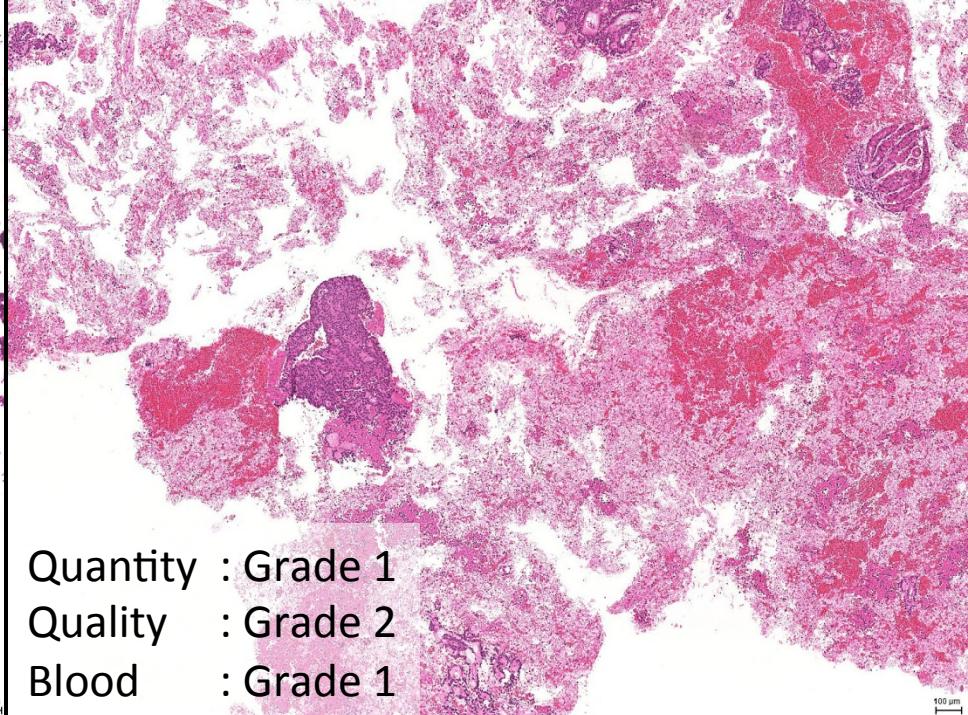


# Pathological Evaluation

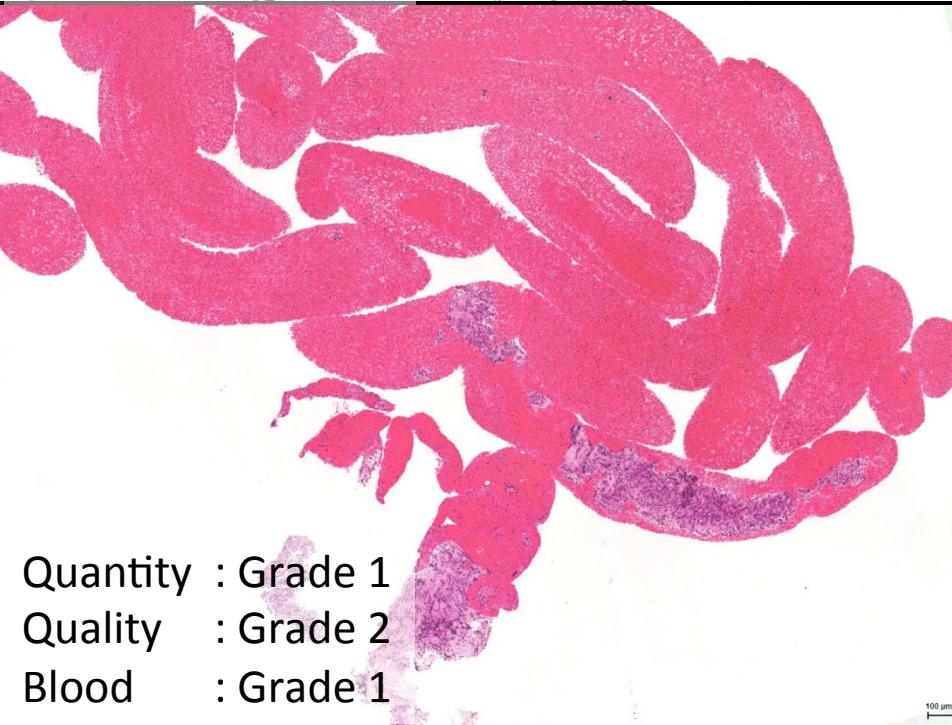
Quantity		
Grade 0	Scant	No or few representative cells
Grade 1	Inadequate	Insufficient amount of representative cells for pathological diagnosis
Grade 2	Adequate	Sufficient amount of representative cells for pathological diagnosis
Quality		
Grade 0	Poor	Fragmented or crushed samples with no histological structure
Grade 1	Moderate	Samples with partially preserved histological structure
Grade 2	Good	Samples with well-preserved histological structure
Blood Contamination		
Grade 0	Significant	Large amount of blood cells making pathological diagnosis difficult
Grade 1	Moderate	Partially obscured by blood cells but pathological diagnosis possible
Grade 2	Low	No or few blood cells with influence on the diagnosis



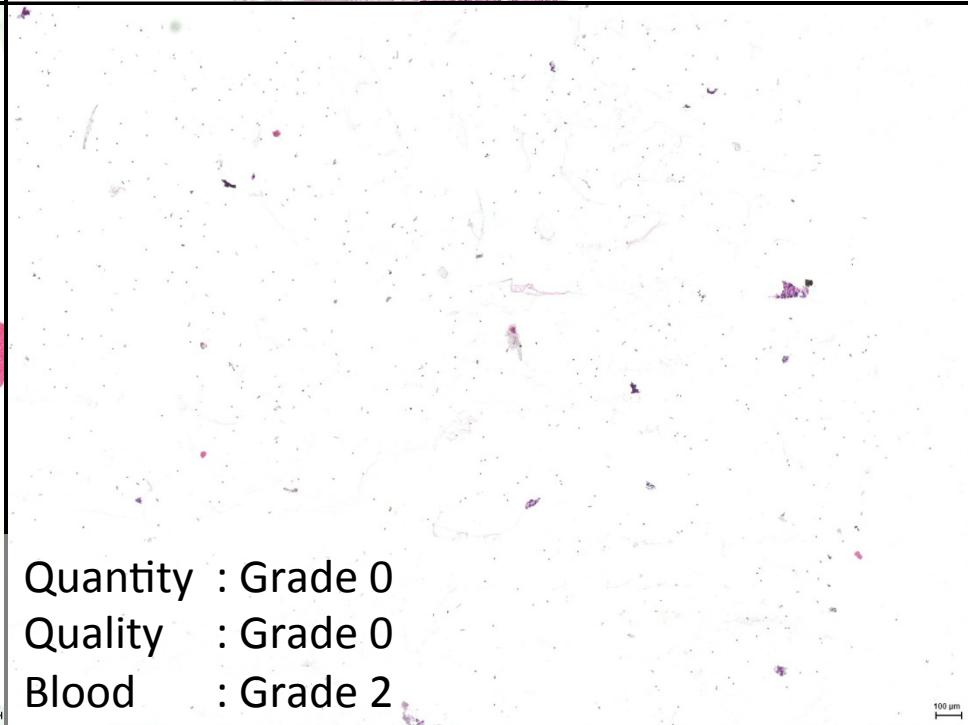
Quantity : Grade 2  
Quality : Grade 2  
Blood : Grade 2



Quantity : Grade 1  
Quality : Grade 2  
Blood : Grade 1



Quantity : Grade 1  
Quality : Grade 2  
Blood : Grade 1



Quantity : Grade 0  
Quality : Grade 0  
Blood : Grade 2

# Sample size estimation

- Primary outcome measure: diagnostic yield
  - Proportion of patients with adequate tissue for diagnosis obtained by EUS FNA
- According to previous studies, the diagnostic yield of MOSE and conventional combined histologic-cytologic analysis were 98.8% and 91.1% respectively.

*Iwashita T, et al. GIE 2015*  
*LeBlanc JK, et al. GIE 2004*

- Assuming a 5% significance level and a power of 80%, a total sample size of 244 (i.e. 122 per group) will be necessary.

# Measurable outcomes

- Primary outcome:

- Diagnostic yield

- Secondary outcomes:

- Number of passes needed for diagnosis
  - Procedure-related complications
  - Sample quality and quantity
  - Sensitivity
  - Specificity
  - Positive predictive value (PPV)
  - Negative predictive value (NPV)
  - Diagnostic accuracy

# Measurable outcomes

- Validate the use of MOSE in EUS FNA

Accurate estimation on adequacy of tissue sample during EUS-FNA in the absence of on-site cytopathologists can avoid additional procedures and the associated risks.

- The results of this study will be presented in the next AEG congress
- Publications in international or local refereed journals
- Reference for setting guidelines, consensus or recommendations in terms of amount of tissue obtained and number of passes needed during EUS FNA

# Milestones

- Sample size: 244
- Accrual rate: ~ 4-6 patients/month/center
- 16 centers → 16 from each center
- 3-4 months to complete the patient accrual

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Jan 2016 Application of IRB

Jun 2016 Start of patients recruitment

Jan 2017 Completion of patients recruitment

Jun 2017 Completion of patients follow-up and Data analysis

Jan 2018 Final Report



# CASE RECORD FORM

Center: \_\_\_\_\_

Randomization number: \_\_\_\_\_



### Case Record Form

## **Macroscopic On-Site Quality Evaluation Of Biopsy Specimens To Improve The Diagnostic Accuracy During EUS-Guided FNA Using A 19-Gauge Needle For Solid Lesions: A Multicenter Double-Blinded Prospective Randomized Controlled Study**

### Patient information

Sex: 1. M      2. F

Age: \_\_\_\_\_

Date of Procedure (dd/mm/yyyy): \_\_\_\_\_

Endoscopic Diagnosis: \_\_\_\_\_

Location of lesion:

1. Pancreas: Head Body Tail Uncinate
2. Subepithelial: Duodenum Stomach
3. Intra-abdominal Lymph node: Porta Celiac Others
4. Adrenal: Right Left
5. Mediastinal
6. Liver
7. Others: \_\_\_\_\_

Size of lesion: \_\_\_\_\_ mm

Puncture: Trans-esophageal Trans-gastric Trans-duodenal

Successful? 1. Yes

2. No      Reason: \_\_\_\_\_

No of passes: \_\_\_\_\_

Total time of procedure: \_\_\_\_\_ minutes

Procedure-related Complication:

- Yes: Please describe: \_\_\_\_\_
- No

**MOSE ARM**

Length of MVC: \_\_\_\_ mm

**Histology Result 1(Bottle 1, MVC)**

Diagnosis can be made: Yes / No / Insufficient material

Diagnosis: \_\_\_\_\_

Quantity	Grade 0 Scant	Grade 1 Inadequate	Grade 2 Adequate
Quality	Grade 0 Poor	Grade 1 Moderate	Grade 2 Good
Blood contamination	Grade 0 Significant	Grade 1 Moderate	Grade 2 Low

**Histology Result 2 (Bottle 2, Red paste-like material)**

Diagnosis can be made: Yes / No/ Insufficient material

Diagnosis: \_\_\_\_\_

Quantity	Grade 0 Scant	Grade 1 Inadequate	Grade 2 Adequate
Quality	Grade 0 Poor	Grade 1 Moderate	Grade 2 Good
Blood contamination	Grade 0 Significant	Grade 1 Moderate	Grade 2 Low

**Cytology Result (Bottle 3, Liquid material)**

Diagnosis can be made: Yes / No/ Insufficient material

Diagnosis: \_\_\_\_\_

Quantity	Grade 0 Scant	Grade 1 Inadequate	Grade 2 Adequate
Quality	Grade 0 Poor	Grade 1 Moderate	Grade 2 Good
Blood contamination	Grade 0 Significant	Grade 1 Moderate	Grade 2 Low

Final Diagnosis: \_\_\_\_\_

Final diagnosis aroused from:

- Surgical specimen for resectable cases.
- Positive FNA diagnosis for malignancy with a compatible clinical course.
- Negative FNA diagnosis for malignancy with a lack of deterioration or spontaneous resolution on radiological studies with a minimum clinical follow-up time of 6 months.

Filled by: \_\_\_\_\_ Signature: \_\_\_\_\_

Control Arm

Histology Result (Bottle 1, MVC + Red paste-like material)

Diagnosis can be made: Yes / No / Insufficient material

Diagnosis: \_\_\_\_\_

Quantity	Grade 0 Scant	Grade 1 Inadequate	Grade 2 Adequate
Quality	Grade 0 Poor	Grade 1 Moderate	Grade 2 Good
Blood contamination	Grade 0 Significant	Grade 1 Moderate	Grade 2 Low

Cytology Result (Bottle 3, Liquid material)

Diagnosis can be made: Yes / No/ Insufficient material

Diagnosis: \_\_\_\_\_

Quantity	Grade 0 Scant	Grade 1 Inadequate	Grade 2 Adequate
Quality	Grade 0 Poor	Grade 1 Moderate	Grade 2 Good
Blood contamination	Grade 0 Significant	Grade 1 Moderate	Grade 2 Low

Final Diagnosis: \_\_\_\_\_

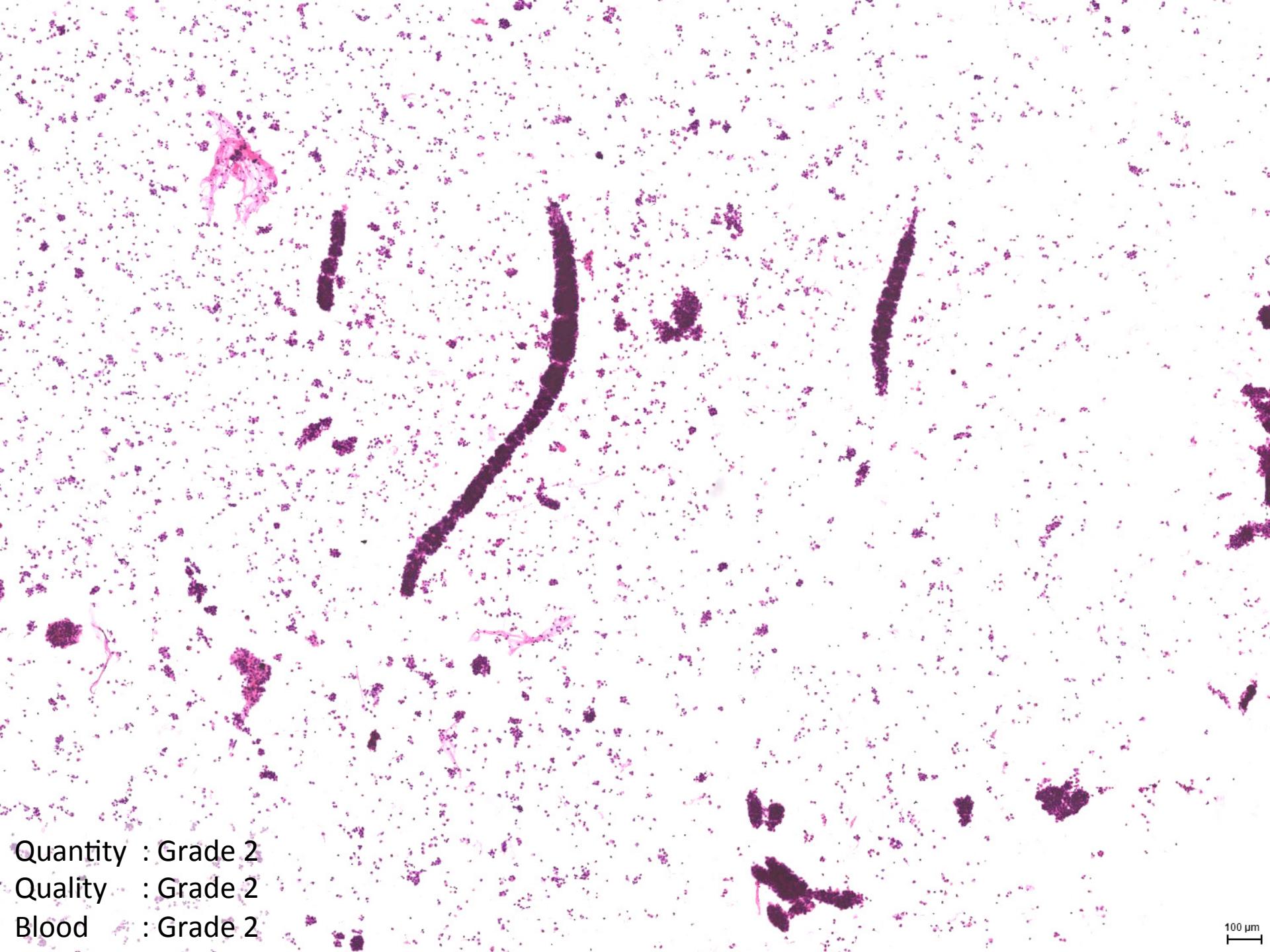
Final diagnosis aroused from:

- o Surgical specimen for resectable cases.
- o Positive FNA diagnosis for malignancy with a compatible clinical course.
- o Negative FNA diagnosis for malignancy with a lack of deterioration or spontaneous resolution on radiological studies with a minimum clinical follow-up time of 6 months.

Filled by: \_\_\_\_\_ Signature: \_\_\_\_\_

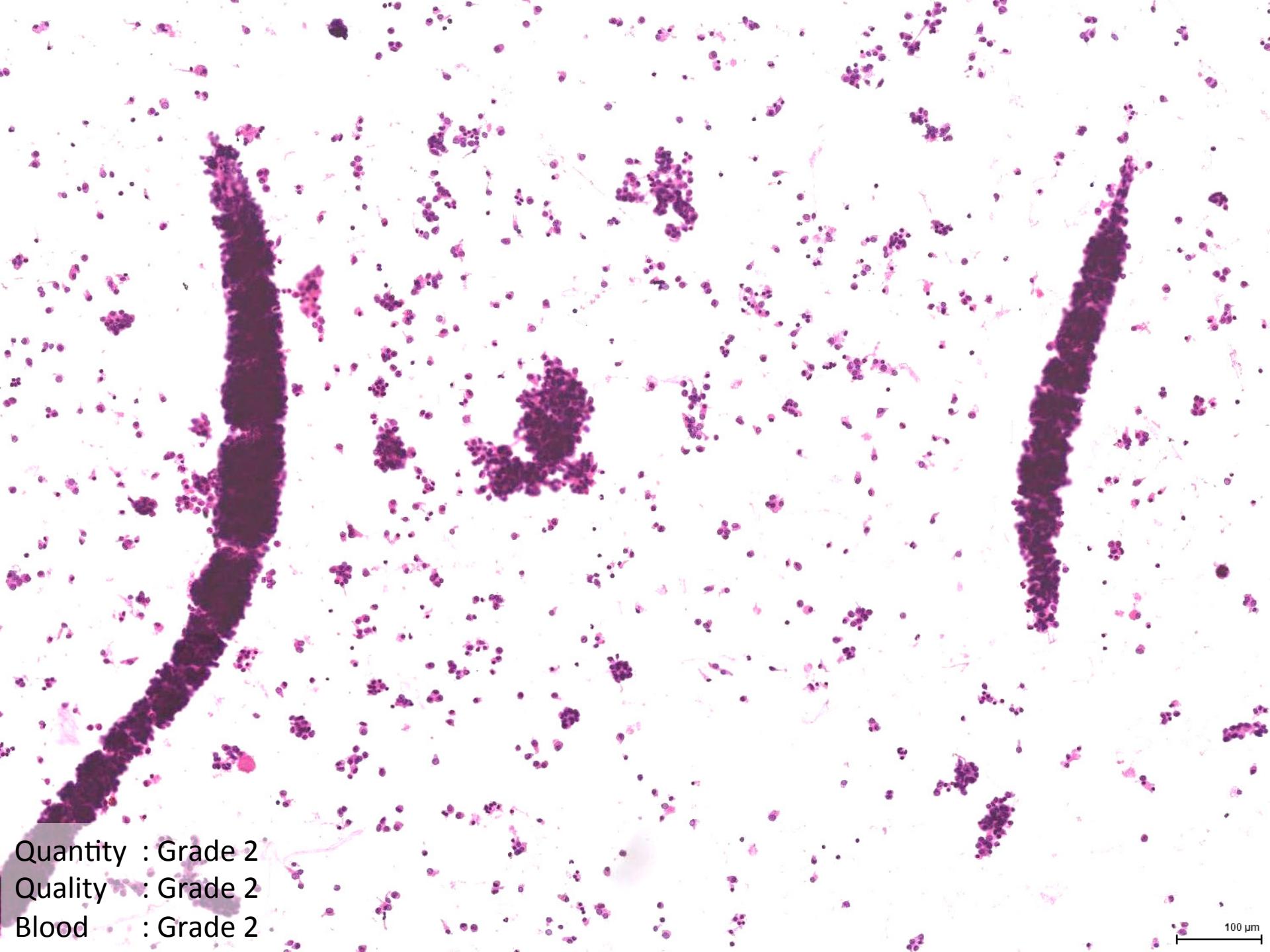


# REFERENCE SLIDES FOR PATHOLOGICAL EVALUATION



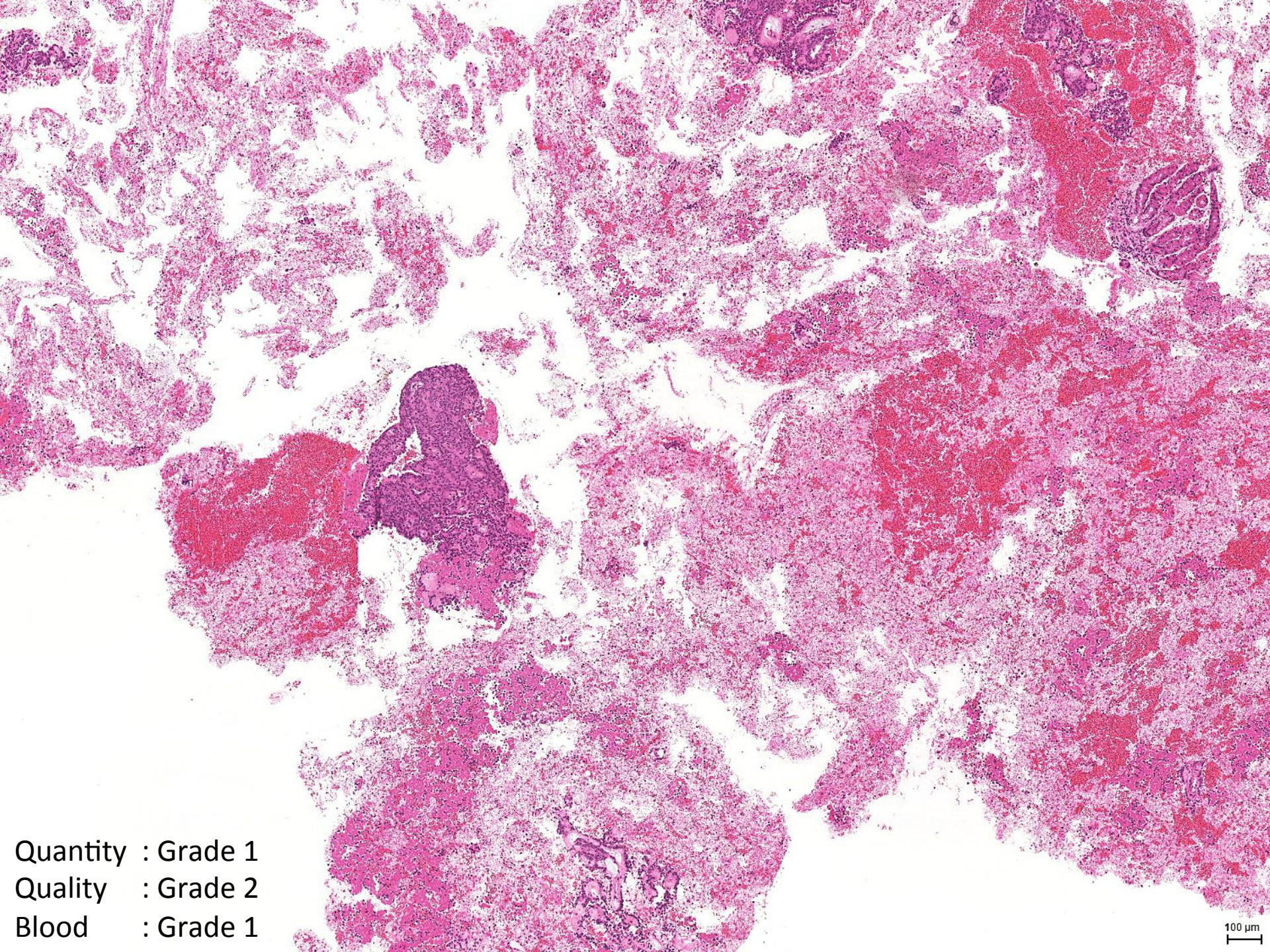
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Quality : Grade 2  
Blood : Grade 2

100 µm



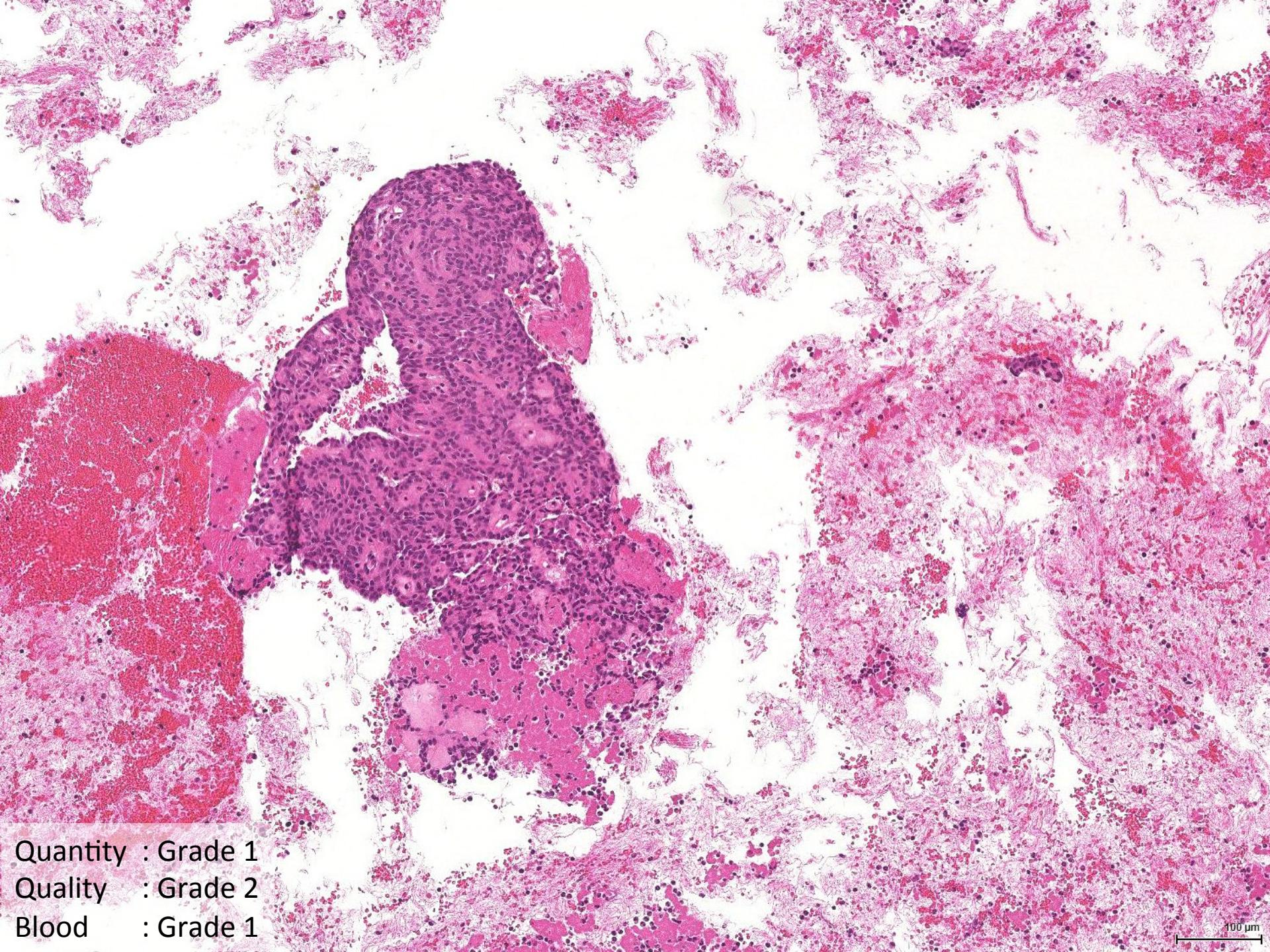
Quantity : Grade 2  
Quality : Grade 2  
Blood : Grade 2

100  $\mu$ m



Quantity : Grade 1  
Quality : Grade 2  
Blood : Grade 1

100 µm



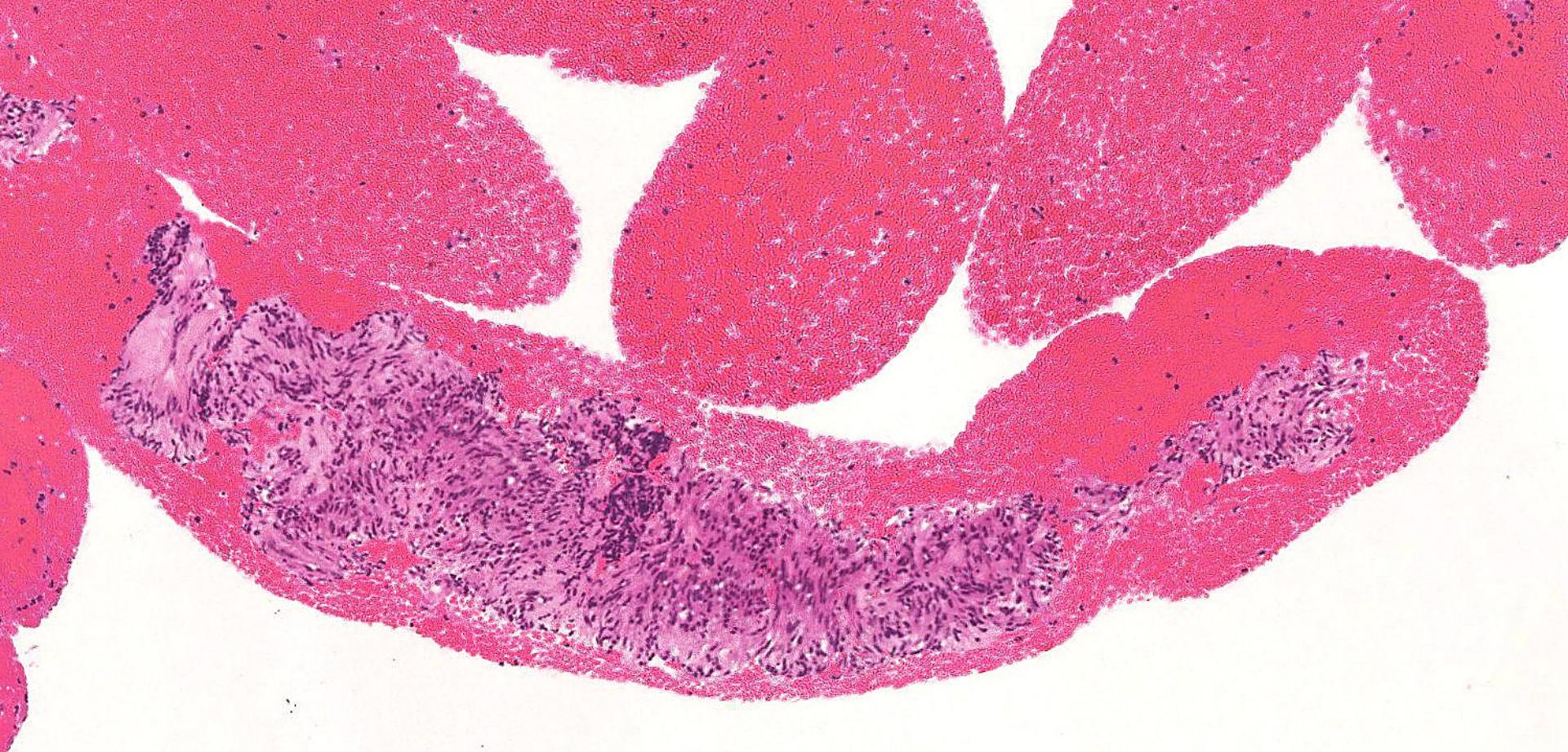
Quantity : Grade 1  
Quality : Grade 2  
Blood : Grade 1

100  $\mu\text{m}$



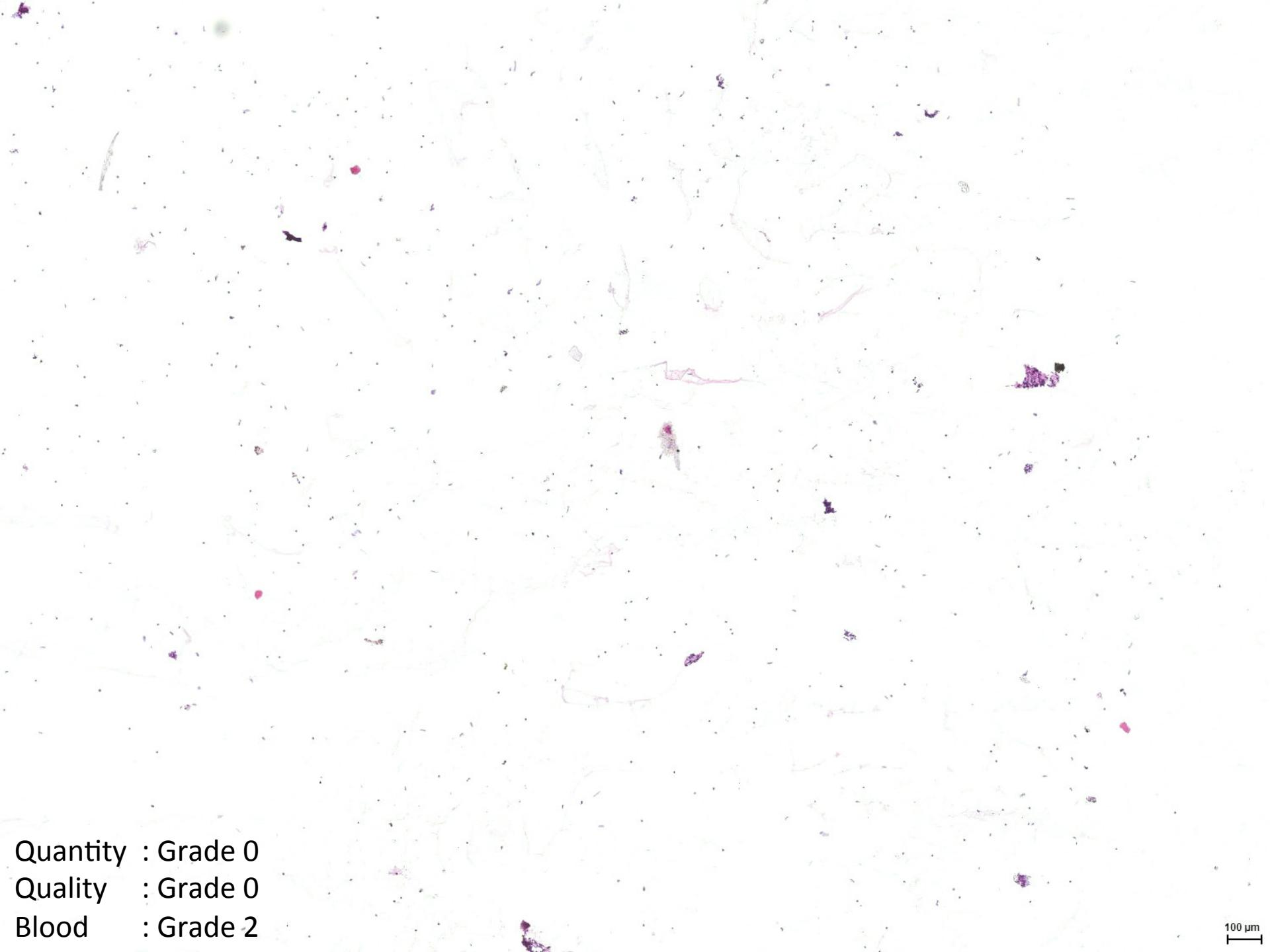
Quantity : Grade 1  
Quality : Grade 2  
Blood : Grade 1

100 µm



Quantity : Grade 1  
Quality : Grade 2  
Blood : Grade 1

100 µm



Quantity : Grade 0  
Quality : Grade 0  
Blood : Grade 2

100 µm