Rapid On-Site Evaluation (ROSE) in Diagnostic Interventional Pulmonology

Volume 4: Metagenomic Sequencing Application in Difficult Cases of Infectious Diseases

Jing Feng Bo Wu Erlie Jiang Wen Li Chen Meng *Editors*



Rapid On-Site Evaluation (ROSE) in Diagnostic Interventional Pulmonology Jing Feng • Bo Wu • Erlie Jiang Wen Li • Chen Meng Editors

Rapid On-Site Evaluation (ROSE) in Diagnostic Interventional Pulmonology

Volume 4: Metagenomic Sequencing Application in Difficult Cases of Infectious Diseases



Editors Jing Feng University General Hospital Tianjin Medical University Tianjin China

Erlie Jiang Peking Union Medical College Chinese Academy of Medical Sciences Beijing China

Chen Meng Qilu Children's hospital Shandong University Jinan China Bo Wu Wuxi People's Hospital Nanjing Medical University Wuxi China

Wen Li Second Affiliated Hospital Zhejiang University Hangzhou China

ISBN 978-981-15-5245-8 ISBN 978-981-15-5246-5 (eBook) https://doi.org/10.1007/978-981-15-5246-5

© Springer Nature Singapore Pte Ltd. 2020

This work is subject to copyright. All rights are reserved by the Publisher, whether the whole or part of the material is concerned, specifically the rights of translation, reprinting, reuse of illustrations, recitation, broadcasting, reproduction on microfilms or in any other physical way, and transmission or information storage and retrieval, electronic adaptation, computer software, or by similar or dissimilar methodology now known or hereafter developed.

The use of general descriptive names, registered names, trademarks, service marks, etc. in this publication does not imply, even in the absence of a specific statement, that such names are exempt from the relevant protective laws and regulations and therefore free for general use.

The publisher, the authors, and the editors are safe to assume that the advice and information in this book are believed to be true and accurate at the date of publication. Neither the publisher nor the authors or the editors give a warranty, expressed or implied, with respect to the material contained herein or for any errors or omissions that may have been made. The publisher remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

This Springer imprint is published by the registered company Springer Nature Singapore Pte Ltd. The registered company address is: 152 Beach Road, #21-01/04 Gateway East, Singapore 189721, Singapore

Preface

The diagnostic interventional pulmonology ROSE is a real-time cytological examination technique, which accompanies sequential sampling. The process of ROSE is as follows: A small part of every tissue specimen sampled from target lesion is smeared on a slide without losing tissue material significantly. Then the cytological slide is stained as soon as possible. Finally, the stained slide is interpreted immediately under specialized microscope integrating with all the available clinical information.

Since 2010, high-tech equipment represented by virtual bronchoscopy (VBN), ultrathin bronchoscopy, endobronchial ultrasound (EBUS), electromagnetic navigation (EMN) bronchoscopy, etc. has been widely used in interventional pulmonary diagnosis and treatment [1, 2]. With these devices and technologies, we can obtain infectious lesions located in the periphery of the lungs. And during the procedures, ROSE can help to evaluate adequate sampling, guide interventional methods and modalities, approach a preliminary diagnosis or narrow differential diagnosis spectrum, optimize processing scheme for target lesion specimen, and analyze patients' disease status and prognosis in combination with all available clinical and cytological information.

After obtaining peripheral pulmonary infectious lesions, these samples can be analyzed by metagenomic next-generation sequencing (mNGS). Using proper reference databases, mNGS can detect pathogenic microbes and marker genes, such as antibiotic resistance genes, potentially increasing the precision of infectious disease diagnosis [3].

This volume includes 107 clinical cases of pulmonary infectious diseases, including CT and brief clinical data of the patients. This volume also provides mNGS results and representative ROSE pictures of these cases. We believe that this content can help readers learn and master ROSE and at the same time deepen readers' knowledge of these infectious diseases.

This book is part of the 4-volume collection *Rapid On-Site Evaluation* (*ROSE*) in *Diagnostic Interventional Pulmonology*. The following contents are important information for ROSE and have been published in chapters in *Rapid On-Site Evaluation* (*ROSE*) in *Diagnostic Interventional Pulmonology*, Volume 1–3.

Chapter 1 (Volume 1–2) Rapid On-Site Evaluation (ROSE) in Diagnostic Interventional Pulmonology: Introduction and Detailed Methods

Jing Feng, Qiang Li, Yi Shi, Ke Wang Pages 1–9

https://linl	c.spri	inger.cor	n/chapter	r/10.1007/97	8-981-13-34	456-6_1	
Volume	1:	Print	ISBN	978-981-1	3-3455-9;	Online	ISBN
978-981-13-3	3456-	-6					
Volume	2:	Print	ISBN	978-981-1	5-0938-4;	Online	ISBN
978-981-15-0)939-	-1					
Chapter 2	2 (Vo	olume 1	-2) Ana	tomic Distri	bution and	Morphol	logy of
Common Tra	chea	l/Bronch	ial/Pulm	onary Cells			
Jing Feng	, Pei	Li, Xin I	Li, Hong	mei Zhou			
Pages 11-	15						
Chapter 3	(Vo	lume 1-	-2) Clust	tering (Categ	gorizing) A	nalysis in	ROSE
Interpretation	n of	Comm	non Nor	nneoplastic	Disease S	states of	Lung/
Mediastinum							
Jing Feng	, Pei	Chen, W	ei Chen,	Yao Li			
Pages 17-	19						
https://linl	c.spri	inger.cor	n/chapter	r/10.1007/97	8-981-13-34	456-6_3	
Chapter 1	(Vo	lume 3)	Cellular	Characteris	tics of ROS	SE in Pul	monary
Solid Malign	ancie	es					
Jing Feng	, Qia	ng Li, H	ongwu W	/ang, Faguan	g Jin, Hong	mei Zhou	
https://doi	.org/	10.1007/	978-981	-15-3910-7_	1		
Print ISBI	N 978	8-981-15	-3909-1;	Online ISBI	N 978-981-	15-3910-7	
Tioniin Chin	0					Lin	ng Feng

Tianjin, China	Jing Feng
Wuxi, China	Bo Wu
Beijing, China	Erlie Jiang
Hangzhou, China	Wen Li
Jinan, China	Chen Meng

References

- Asano F, Eberhardt R, Herth FJ. Virtual bronchoscopic navigation for peripheral pulmonary lesions. Respiration. 2014;88(5):430–40. doi: 10.1159/000367900. Review. PubMed PMID: 25402610.
- Zaric B, Stojsic V, Sarcev T, Stojanovic G, Carapic V, Perin B, Zarogoulidis P, Darwiche K, Tsakiridis K, Karapantzos I, Kesisis G, Kougioumtzi I, Katsikogiannis N, Machairiotis N, Stylianaki A, Foroulis CN, Zarogoulidis K. Advanced bronchoscopic techniques in diagnosis and staging of lung cancer. J Thorac Dis. 2013;5 Suppl 4:S359–70. doi: 10.3978/j.issn.2072-1439.2013.05.15. Review. PubMed PMID: 24102008; PubMed Central PMCID: PMC3791497.
- Liu N, Kan J, Cao W, Cao J, Jiang E, Zhou Y, Zhao M, Feng J. Metagenomic next-generation sequencing diagnosis of peripheral pulmonary infectious lesions through virtual navigation, radial EBUS, ultrathin bronchoscopy, and ROSE. J Int Med Res. 2019;47(10):4878–85. doi: 10.1177/0300060519866953. Epub 2019 Aug 22. PubMed PMID: 31436107; PubMed Central PMCID: PMC6833387. From our team.

Contents

1	Tuberculosis 1Jing Feng, Bo Wu, Erlie Jiang, Wen Li, and Chen Meng
2	Non-tuberculous Mycobacterium Infections51Jing Feng, Bo Wu, Erlie Jiang, Wen Li, and Chen Meng
3	Bacterial Pneumonia.57Jing Feng, Bo Wu, Erlie Jiang, Wen Li, and Chen Meng
4	Viral Pneumonia87Jing Feng, Bo Wu, Erlie Jiang, Wen Li, and Chen Meng
5	Pulmonary Cryptococcosis
6	<i>Pneumocystis jirovecii</i> Pneumonia
7	Pulmonary Aspergillosis163Jing Feng, Bo Wu, Erlie Jiang, Wen Li, and Chen Meng
8	Pulmonary Mucormycosis223Jing Feng, Bo Wu, Erlie Jiang, Wen Li, and Chen Meng
9	Other Mycotic Pneumonia
10	Pulmonary Mixed Infections287Jing Feng, Bo Wu, Erlie Jiang, Wen Li, and Chen Meng
11	Other Pathogen Infections
12	Noninfectious Diseases Mainly

Tuberculosis

Jing Feng, Bo Wu, Erlie Jiang, Wen Li, and Chen Meng

1.1 Introduction

Tuberculosis (TB) is an airborne infectious disease caused by organisms of the *Mycobacterium tuberculosis* complex, mainly *Mycobacterium tuberculosis*. *Mycobacterium tuberculosis* is a rod-shaped, nonmotile, slow-growing, acid-fast bacterium. TB transmission occurs when a contagious patient coughs, spreading bacilli through the air. Although primarily a pulmonary pathogen, it can affect any organ in the body. If not treated properly, TB disease can be fatal.

J. Feng (🖂)

University General Hospital, Tianjin Medical University, Tianjin, China e-mail: zyyhxkfj@126.com

B. Wu Wuxi People's Hospital, Nanjing Medical University, Wuxi, China e-mail: fyz333@126.com

E. Jiang

Peking Union Medical College, Chinese Academy of Medical Sciences, Beijing, China e-mail: jiangerlie@163.com

W. Li Second Affiliated Hospital, Zhejiang University, Hangzhou, China e-mail: liwen@zju.edu.cn

C. Meng Qilu Children's Hospital, Shandong University, Jinan, China e-mail: mengchen.6666@163.com This section contains 14 clinical cases of tuberculosis, including 11 cases of pulmonary tuberculosis, 1 case of endobronchial tuberculosis, and 2 cases of mediastinal lymphonode tuberculosis. This part can make readers understand the disease more deeply.

1.2 Final Diagnosis: Clinically Diagnosed as Pulmonary Tuberculosis

Brief history

Gender: Male; Age: 22 years old; a patient with preexisting acute lymphocytic leukemia receiving chemotherapy; Persistent coughing.

Technology to obtain the target lesions: transbronchial lung biopsy (TBLB)

Technology to obtain the target lesions: bronchoalveolar lavage

The preparation of cytological slides for ROSE: imprinting (rolling)

Imaging Features

Consolidation; Exudation.

Nodule or mass; Pleural thickening.

Clustering (categorizing) analysis in ROSE interpretation:

- "Inflammatory changes"
- Granulomatous inflammation
- Lymphocyte-based immune inflammatory response

Check for updates

[©] Springer Nature Singapore Pte Ltd. 2020

J. Feng et al. (eds.), *Rapid On-Site Evaluation (ROSE) in Diagnostic Interventional Pulmonology*, https://doi.org/10.1007/978-981-15-5246-5_1



Fig. 1.1 (a, b) CT/X-ray/PET-CT



Fig. 1.2 (**a**–**e**) Annotated at the figure (yellow arrow)

PCR GeneXpert Dx System (Bacillus tuberculosis typus humanus): bronchoalveolar lavage (+)

Results of Next-generation sequencing (NGS) Bronchoalveolar lavage: *Mycobacterium tuberculosis* 110 copies

1.3 Final Diagnosis: Clinically Diagnosed as Pulmonary Tuberculosis

Brief history

Gender: Male; Age: 55 years old; Persistent coughing; Hemoptysis (blood-stained sputum).

Technology to obtain the target lesions: transbronchial lung biopsy (TBLB)

The preparation of cytological slides for ROSE: imprinting (rolling)

Imaging Features

Patches; Exudation.

Cavity; Calcification.

Clustering (categorizing) analysis in ROSE interpretation:

- Suppurative infections (with or without visible pathogens)
- Granulomatous inflammation
- Necrotic "Inflammatory changes"

PCR GeneXpert Dx System (Bacillus tuberculosis typus humanus): bronchoalveolar lavage (+)

Results of Next-generation sequencing (NGS) Transbronchial lung biopsy (TBLB): *Mycobacterium tuberculosis* 4074 copies



Fig. 1.3 (a, b) CT/X-ray/PET-CT



Fig. 1.3 (continued)



Fig. 1.4 (**a**–**e**) Annotated at the figure (yellow arrow)



Fig. 1.4 (continued)

1.4 Final Diagnosis: Clinically Diagnosed as Pulmonary Tuberculosis

Brief history

Gender: Male; Age: 77 years old; a patient with preexisting chronic lymphocytic leukemia

receiving chemotherapy; Persistent coughing; Shortness of breath; Running a fever.

Technology to obtain the target lesions: transbronchial lung biopsy (TBLB)

Technology to obtain the target lesions: transbronchial brushing (TBBr)

Technology to obtain the target lesions: bronchoalveolar lavage (BAL)

The guiding pattern for TBLB: Joint application of virtual navigation, radial EBUS, ultrathin bronchoscopy and ROSE

The preparation of cytological slides for ROSE: imprinting (rolling)

Patches; Consolidation; Exudation; Tree-inbud sign.

Nodule or mass.

Clustering (categorizing) analysis in ROSE interpretation:

- "Inflammatory changes"
- Granulomatous inflammation
- Necrotic "Inflammatory changes"

PCR GeneXpert Dx System (Bacillus tuberculosis typus humanus): bronchoalveolar lavage (+)

Results of microbial Next-generation sequencing (NGS)

Test 1 DNA

Transbronchial lung biopsy (TBLB): *Mycobacterium tuberculosis* complex 152 copies

Transbronchial brushing (TBBr): *Mycobacterium tuberculosis* complex 265 copies

Bronchoalveolar lavage: *Mycobacterium tuberculosis* complex 472 copies



Fig. 1.5 (a–d) Imaging Features



Fig. 1.6 (**a**–**e**) Annotated at the figure (yellow arrow)



Fig. 1.6 (continued)

1.5 Final Diagnosis: Clinically Diagnosed as Pulmonary Tuberculosis

Brief history

Gender: Female; Age: 50 years old; Persistent coughing.

Technology to obtain the target lesions: transbronchial lung biopsy (TBLB)

Technology to obtain the target lesions: transbronchial brushing (TBBr)

Technology to obtain the target lesions: bronchoalveolar lavage (BAL)

The guiding pattern for TBLB: Joint application of virtual navigation, radial EBUS, ultrathin bronchoscopy and ROSE

The preparation of cytological slides for ROSE: imprinting (rolling)

Patches; Tree-in-bud sign.

Clustering (categorizing) analysis in ROSE interpretation:

- "Inflammatory changes"
- Suppurative infections (with or without visible pathogens)
- Granulomatous inflammation
- Necrotic "Inflammatory changes"

PCR GeneXpert Dx System (Bacillus tuberculosis typus humanus): bronchoalveolar lavage (+)

Results of microbial Next-generation sequencing (NGS)

Test 1

Transbronchial lung biopsy (TBLB): *Mycobacterium tuberculosis* complex 2 copies

Mixed specimens from the following technologies for obtaining the target lesions: *Mycobacterium tuberculosis* complex 3 copies

Transbronchial brushing (TBBr); Bronchoalveolar lavage







Fig. 1.8 (**a**–**e**) Annotated at the figure (yellow arrow)



Fig. 1.8 (continued)

1.6 Final Diagnosis: Clinically Diagnosed as Pulmonary Tuberculosis

Brief history

Gender: Male; Age: 67 years old; Persistent coughing.

Technology to obtain the target lesions: transbronchial lung biopsy (TBLB)

Technology to obtain the target lesions: transbronchial brushing (TBBr)

Technology to obtain the target lesions: bronchoalveolar lavage (BAL)

The guiding pattern for TBLB: Joint application of virtual navigation, radial EBUS, ultrathin bronchoscopy and ROSE

The preparation of cytological slides for ROSE: imprinting (rolling)

Patches; Consolidation; Exudation; Tree-inbud sign.

Clustering (categorizing) analysis in ROSE interpretation:

- "Inflammatory changes"
- Granulomatous inflammation
- Necrotic "Inflammatory changes"

PCR GeneXpert Dx System (Bacillus tuberculosis typus humanus): bronchoalveolar lavage (+)

Results of microbial Next-generation sequencing (NGS)

Test 1

Bronchoalveolar lavage: *Mycobacterium tuberculosis* complex 30 copies



Fig. 1.9 (a–d) Imaging Features



Fig. 1.9 (continued)



Fig. 1.10 (a–e) Annotated at the figure (yellow arrow)



Fig. 1.10 (continued)

1.7 Final Diagnosis: Clinically Diagnosed as Pulmonary Tuberculosis

Brief history

Gender: Male; Age: 52 years old; a patient with preexisting acute lymphocytic leukemia

receiving peripheral blood stem cell transplantation (PBSCT); Persistent coughing; Shortness of breath; Running a fever.

Technology to obtain the target lesions: transbronchial lung biopsy (TBLB)

Technology to obtain the target lesions: transbronchial brushing (TBBr)

Technology to obtain the target lesions: bronchoalveolar lavage (BAL)

The guiding pattern for TBLB: Joint application of virtual navigation, radial EBUS, ultrathin bronchoscopy and ROSE

The preparation of cytological slides for ROSE: imprinting (rolling)

Consolidation; Tree-in-bud sign.

Clustering (categorizing) analysis in ROSE interpretation:

Granulomatous inflammation

PCR GeneXpert Dx System (Bacillus tuberculosis typus humanus): bronchoalveolar lavage (+)

Results of microbial Next-generation sequencing (NGS)

Test 1

Transbronchial lung biopsy (TBLB): Mycobacterium tuberculosis complex 1 copy

Mixed specimens from the following technologies for obtaining the target lesions: *Mycobacterium tuberculosis* complex 2 copies

Transbronchial brushing (TBBr); Bronchoalveolar lavage



Fig. 1.11 (a–d) Imaging Features



Fig. 1.12 (a, b) Annotated at the figure (yellow arrow)

1.8 Final Diagnosis: Clinically Diagnosed as Pulmonary Tuberculosis

Brief history

Gender: Female; Age: 39 years old; a patient with preexisting acute myeloid leukemia receiving peripheral blood stem cell transplantation (PBSCT); Persistent coughing; Running a fever.

Technology to obtain the target lesions: transbronchial lung biopsy (TBLB)

Technology to obtain the target lesions: transbronchial brushing (TBBr)

Technology to obtain the target lesions: bronchoalveolar lavage (BAL)

The guiding pattern for TBLB: Joint application of virtual navigation, radial EBUS, ultrathin bronchoscopy and ROSE The preparation of cytological slides for ROSE: imprinting (rolling)

Consolidation; Exudation; Calcification.

Nodule or mass.

Clustering (categorizing) analysis in ROSE interpretation:

• Granulomatous inflammation

PCR GeneXpert Dx System (Bacillus tuberculosis typus humanus): bronchoalveolar lavage (+)

Test 1 DNA

Transbronchial lung biopsy (TBLB): Mycobacterium tuberculosis complex 684 copies

Bronchoalveolar lavage: *Mycobacterium tuberculosis* complex 682 copies



Fig. 1.13 (a–d) Imaging Features



Fig. 1.14 (a–e) Annotated at the figure (yellow arrow)

Fig. 1.14 (continued)

1.9 **Final Diagnosis: Clinically Diagnosed as Pulmonary Tuberculosis**

Brief history

Gender: Male; Age: 67 years old; Persistent coughing; Hemoptysis (blood-stained sputum); Running a fever.

Technology to obtain the target lesions: transbronchial lung biopsy (TBLB)

Technology to obtain the target lesions: transbronchial brushing (TBBr)

Technology to obtain the target lesions: bronchoalveolar lavage (BAL)

The guiding pattern for TBLB: Joint application of virtual navigation, radial EBUS, ultrathin bronchoscopy and ROSE

The preparation of cytological slides for ROSE: imprinting (rolling)

Consolidation; Exudation

Cavity or air containing space lesion; Central low attenuation; Pleural thickening.

Clustering (categorizing) analysis in ROSE interpretation:

- Granulomatous infla
- ory changes"

PCR GeneXpert Dx System (Bacillus tuberculosis typus humanus): bronchoalveolar lavage (+)

Results of microbial Next-generation sequencing (NGS)

Test 1 DNA

Transbronchial (TBLB): lung biopsy *Mycobacterium* tuberculosis complex 864 copies

Bronchoalveolar lavage: *Mycobacterium* tuberculosis complex 58 copies





Fig. 1.15 (a–d) Imaging Features