COVIDIEN

510(k) Summary K130357
Covidien llc, dba superDimension Inc.
SuperDimension® Triple Needle Cytology Brush

Date Prepared: 11/4/2013

510(k) Applicant: Covidien llc, formerly registered as superDimension Inc.
161 Cheshire Lane Suite 100
Plymouth, MN 55441 U.S.A.

Contract Person: Deborah Fleetham , Manager Regulatory Affairs
Phone: 763-210-4091
Fax: 763-210-4098
Email : deborah.fleetham@covidien.com

Name of Device :

Trade Name :	superDimension® Triple Needle Cytology Brush
Common Name:	Bronchial Biopsy Brush
Classification Name:	Bronchoscope (flexible or rigid) and accessories 21 CFR Part 874.4680
Product code:	BTG

Equivalent Legally-Marketed Devices:
K834402 Gastrointestinal Sheath Brush (KOG) by Hobbs Medical, Inc.
K944650 Wang Bronchial Needle Brush (EOQ) by ConMed

Description:
The superDimension® Triple Needle Cytology Brush is designed to obtain tissue samples for biopsy from endobronchial lesions, peripheral lung nodules, or lung masses. The superDimension® Triple Needle Cytology Brush is an endoscopic catheter comprised of an outer Ethylene Tetrafluoroethylene (ETFE) sheathing and an inner catheter assembly. The inner catheter assembly consists of a thumb ring at the proximal end and a twisted wire shaft to connect to the distal end. The distal end terminates in three connected brushes available in two lengths: 10 mm and 15mm. The brushes have sharpened ends, referred to as needle-tipped, that can be used to rough up tissue to obtain a sample of tissue or cells. When the catheter is inserted into a channel such as a bronchoscope or superDimension Extended Working Channel (EWC) with the distal brush in a retracted position inside the outer sheath. When the catheter is in position, the brushes can be extended into the tissue to obtain tissue samples by advancing the proximal thumb ring. When the physician believes that an adequate sample has been taken, the brushes are retracted back into the sheath and then the entire catheter is withdrawn from the channel for standard tissue analysis. The superDimension® Triple Needle Cytology Brush is similar to currently marketed cytology brushes except that it has three smaller brushes in place of one larger brush.

Intended Use:
To be utilized through a flexible endoscope or the superDimension system by physicians who are trained in endoscopic techniques for retrieving specimens from patients with endobronchial lesions, peripheral lung nodules, or lung masses.

Summary of Substantial Equivalence:
The superTrax Triple Needle-Tipped Cytology brush is substantially equivalent to the ConMed Needle-Tipped Cytology Brush and the Hobbs Cytology Brush predicate devices in the following attributes:

- Indications for Use
- Mechanism of action
- Length
- Sterilization technique
- Performance Characteristics
- Design
- Size
- Materials
- Packaging

The difference between the predicate devices and the superDimension Triple Needle Cytology Brush is that the predicate devices have one, larger brush on the distal end compared to three smaller, flexible brushes on the distal end of the superDimension Triple Needle Cytology Brush.

Performance Data:
In-vitro and in-vivo testing has been performed on all components, subassemblies, and /or full devices. The results showed that the device met the required specifications for the completed tests and performed similarly to the predicate devices. Testing included the following:

- In Vitro Testing
  - Radiographic Testing
  - Catheter Tensile Testing
  - Dimensional Testing
  - Simulated Use Testing
  - Trackability Testing
  - Shelf Life Testing per ASTM F1980-07, ASTM F2096-11, and ASTM F88-09
  - Distribution Testing per ASTM D4169-09
  - Sterilization Testing per ISO 11135-1
  - Biocompatibility Testing (cytotoxicity, irritation, sensitization) per ISO 10993-1, ISO 10993-5, ISO 10993-7, ISO 10993-10
- In Vivo Testing in a porcine model
  - Tissue Collection
  - Safety Testing

Clinical Data:
Clinical tests were not required to validate the design of the SuperDimension® Triple Needle Cytology Brush due to the extensive history of similar devices.

Conclusion:

Based on the intended use, technological characteristics, and results from safety and performance testing, the superDimension Triple Needle Cytology Brush is substantially equivalent to the legally marketed predicate devices, Gastrointestinal Sheath Brush (KOG) by Hobbs Medical, Inc. K834402, and the Wang Bronchial Needle Brush (EOQ) by ConMed K944650.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center - WO66-G609
Silver Spring, MD 20993-002

November 6, 2013

Covidien Llc
c/o Ms. Deborah Fleetham
Manager, Regulatory Affairs
161 Cheshire Lane, Suite 100
Minneapolis, MN 55441

Re: K130357
Trade/Device Name: Superdimension Triple-Needle Cytology Brush
Regulation Number: 21 CFR 874.4680
Regulation Name: Bronchoscope (Flexible or Rigid) and Accessories
Regulatory Class: Class II
Product Code: BTG
Dated: September 27, 2013
Received: September 30, 2013

Dear Ms. Fleetham:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please go to http://www.fda.gov/AboutFDA/CentersOffices/CDRH/CDRHOffices/ucm115809.htm for the Center for Devices and Radiological Health's (CDRH's) Office of Compliance. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Eric A. Mann -S

for Malvina B. Eydelman, M.D.
Director
Division of Ophthalmic and Ear, Nose
and Throat Devices
Office of Device Evaluation
Center for Devices and Radiological Health

Enclosure

Indications for Use

510(k) Number (if known): K130357

Device Name: superDimension® Triple Needle Cytology Brush

Indications For Use:

To be utilized through a flexible endoscope or the superDimension system by physicians who are trained in endoscopic techniques for retrieving specimens from patients with endobronchial lesions, peripheral lung nodules, or lung masses.

Prescription Use __X___ AND/OR Over-The-Counter Use _____
(Part 21 CFR 801 Subpart D) (21 CFR 807 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE - CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of Center for Devices and Radiological Health (CDRH)

Sunny Park

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center - WO66-G609
Silver Spring, MD 20993-002

November 6, 2013

Covidien Llc
c/o Ms. Deborah Fleetham
Manager, Regulatory Affairs
161 Cheshire Lane, Suite 100
Minneapolis, MN 55441

Re: K130357
Trade/Device Name: Superdimension Triple-Needle Cytology Brush
Regulation Number: 21 CFR 874.4680
Regulation Name: Bronchoscope (Flexible or Rigid) and Accessories
Regulatory Class: Class II
Product Code: BTG
Dated: September 27, 2013
Received: September 30, 2013

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If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

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Sincerely yours,

Eric A. Mann -S

for Malvina B. Eydelman, M.D.
Director
Division of Ophthalmic and Ear, Nose
and Throat Devices
Office of Device Evaluation
Center for Devices and Radiological Health

Enclosure

Concurrence & Template History Page

Full Submission Number: **K130357/S001**

For Office of Compliance Contact Information:

http://insideportlets.fda.gov:9010/portal/page?_pageid=197,415881&_dad=portal&_schema=PORTAL&org=318

For Office of Surveillance and Biometrics Contact Information:

http://insideportlets.fda.gov:9010/portal/page?_pageid=197,415881&_dad=portal&_schema=PORTAL&org=423

Digital Signature Concurrence Table	
Reviewer Sign-Off	Sunny Park, Ph.D. 11/6/13
Branch Chief Sign-Off	Srinivas Nandkumar, Ph.D. 11/6/13
Division Sign-Off	Eric A. Mann -S 2013.11.06 10:45:58 -05'00'

Template Name: K1(A) – SE after 1996

Template History:

Date of Update	By	Description of Update
7/27/09	Brandi Stuart	Added Updates to Boiler Table
8/7/09	Brandi Stuart	Updated HFZ Table
1/11/10	Diane Garcia	Liability/Warranty sentence added at bottom of 1st page
10/4/11	M. McCabe Janicki	Removed IFU sheet and placed in Forms
9/25/12	Edwena Jones	Added digital signature format

Typed: Marisol Lendor – November 6, 2013

Indications for Use

510(k) Number (if known): K130357

Device Name: superDimension® Triple Needle Cytology Brush

Indications For Use:

To be utilized through a flexible endoscope or the superDimension system by physicians who are trained in endoscopic techniques for retrieving specimens from patients with endobronchial lesions, peripheral lung nodules, or lung masses.

Prescription Use X AND/OR Over-The-Counter Use _____
(Part 21 CFR 801 Subpart D) (21 CFR 807 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE - CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of Center for Devices and Radiological Health (CDRH)

Sunny Park

K130357

COVIDIEN

February 12, 2013

Food and Drug Administration
Center for Devices and Radiological Health
Document Mail Center
10903 New Hampshire Ave. Bldg 66 room G609
Silver Spring, MD 20993-0002

Re: 510(k) Notification for the superTrax® Triple-Needle tipped Cytology Brush

Attention: Document Mail Clerk

This Traditional 510(k) is being submitted to notify you of the intention of Covidien llc, formerly registered as superDimension Inc. (the 510(k) Applicant) to introduce a new Cytology Brush for use in bronchial applications. This cytology brush is substantially equivalent to existing products on the market except that instead of a single brush on the distal end, there are three smaller brushes. The information below provides the basic identity of the product and applicant.

Common name:	Bronchial Biopsy Brush
Proprietary Name:	superTrax® Triple Needle-Tipped Cytology Brush
Classification:	Class II – CFR 874.4680
Classification Name:	Brush, Biopsy, Bronchoscope (non-rigid)
Product Code:	BTG
Manufactured At:	Covidien llc, formerly registered as superDimension Inc.

Establishment Registration Number: 3004962788

There are no applicable special controls for this device.

In addition to the required sections of the 510(k), an additional section, Desired Claims, has been added to document the claims that Covidien llc would like to use in marketing literature.

This paper copy is accompanied by an eCopy which is an exact duplicate of the paper copy.

510(k) Applicant:
Deborah Fleetham
Manager, Regulatory Affairs
Covidien llc
161 Cheshire Lane, Suite 100
Minneapolis, MN 55441

Please direct all questions or correspondence to the 510(k) Application Correspondent listed below.

510(k) Application Correspondent:
Kristen Swanson
Regulatory Affairs Consultant
Prepared for Covidien llc
161 Cheshire Lane, Suite 100
Minneapolis, MN 55441
Phone: 763-210-4062
Fax: 763-210-4098
Email: kristen.swanson@covidien.com

Sincerely,

Deborah Fleetham

Deborah Fleetham
Manager, Regulatory Affairs
Phone: 763-210-4091
Fax: 763-210-4098
Email: deborah.fleetham@covidien.com

Form Approved: OMB No. 0910-511 Expiration Date: February 28, 2013. See Instructions for OMB Statement.

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION
MEDICAL DEVICE USER FEE COVER SHEET

PAYMENT IDENTIFICATION NUMBER (b) (4) [redacted]
Write the Payment Identification number on your check.

A completed cover sheet must accompany each original application or supplement subject to fees. If payment is sent by U.S. mail or courier, please include a copy of this completed form with payment. Payment and mailing instructions can be found at: http://www.fda.gov/oc/mdufma/coversheet.html

1. COMPANY NAME AND ADDRESS (include name, street address, city state, country, and post office code)

Covidien LLC
161 CHESHIRE LANE
MINNEAPOLIS MN 554415433
US

1.1 EMPLOYER IDENTIFICATION NUMBER (EIN)
*****0868

2. CONTACT NAME
Kristen Swanson
2.1 E-MAIL ADDRESS
kristen.swanson@covidien.com
2.2 TELEPHONE NUMBER (include Area code)
763-2104062
2.3 FACSIMILE (FAX) NUMBER (Include Area code)
800-3879016

3. TYPE OF PREMARKET APPLICATION (Select one of the following in each column; if you are unsure, please refer to the application descriptions at the following web site: http://www.fda.gov/oc/mdufma

Select an application type:
[X] Premarket notification(510(k)); except for third party
[ ] 513(g) Request for Information
[ ] Biologics License Application (BLA)
[ ] Premarket Approval Application (PMA)
[ ] Modular PMA
[ ] Product Development Protocol (PDP)
[ ] Premarket Report (PMR)
[ ] Annual Fee for Periodic Reporting (APR)
[ ] 30-Day Notice

3.1 Select a center
[X] CDRH
[ ] CBER

3.2 Select one of the types below
[X] Original Application

Supplement Types:
[ ] Efficacy (BLA)
[ ] Panel Track (PMA, PMR, PDP)
[ ] Real-Time (PMA, PMR, PDP)
[ ] 180-day (PMA, PMR, PDP)

4. ARE YOU A SMALL BUSINESS? (See the instructions for more information on determining this status)
[ ] YES, I meet the small business criteria and have submitted the required qualifying documents to FDA
[X] NO, I am not a small business
4.1 If Yes, please enter your Small Business Decision Number:

5. FDA WILL NOT ACCEPT YOUR SUBMISSION IF YOUR COMPANY HAS NOT PAID AN ESTABLISHMENT REGISTRATION FEE THAT IS DUE TO FDA. HAS YOUR COMPANY PAID ALL ESTABLISHMENT REGISTRATION FEES THAT ARE DUE TO FDA?
[X] YES (All of our establishments have registered and paid the fee, or this is our first device, and we will register and pay the fee within 30 days of FDA's approval/clearance of this device.)
[ ] NO (If "NO," FDA will not accept your submission until you have paid all fees due to FDA. This submission will not be processed; see http://www.fda.gov/cdrh/mdufma for additional information)

6. IS THIS PREMARKET APPLICATION COVERED BY ANY OF THE FOLLOWING USER FEE EXCEPTIONS? IF SO, CHECK THE APPLICABLE EXCEPTION.
[ ] This application is the first PMA submitted by a qualified small business, including any affiliates
[ ] This biologics application is submitted under section 351 of the Public Health Service Act for a product licensed for further manufacturing use only
[ ] The sole purpose of the application is to support conditions of use for a pediatric population
[ ] The application is submitted by a state or federal government entity for a device that is not to be distributed commercially

7. IS THIS A SUPPLEMENT TO A PREMARKET APPLICATION FOR WHICH FEES WERE WAIVED DUE TO SOLE USE IN A PEDIATRIC POPULATION THAT NOW PROPOSES CONDITION OF USE FOR ANY ADULT POPULATION? (If so, the application is subject to the fee that applies for an original premarket approval application (PMA).
[ ] YES [X] NO

PAPERWORK REDUCTION ACT STATEMENT
Public reporting burden for this collection of information is estimated to average 18 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden, to the address below.

Department of Health and Human Services, Food and Drug Administration, Office of Chief Information Officer, 1350 Piccard Drive, 4th Floor Rockville, MD 20850
[Please do NOT return this form to the above address, except as it pertains to comments on the burden estimate.]

(b) (4) [redacted]
NT AMOUNT SUBMITTED FOR THIS PREMARKET APPLICATION

07-Feb-2013

"Close Window" Print Cover sheet

Kristen Swanson 07 Feb 2013

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

CDRH PREMARKET REVIEW SUBMISSION COVER SHEET

Form Approval
OMB No. 0910-0120
Expiration Date: December 31, 2013
See OMB Statement on page 5.

Date of Submission	User Fee Payment ID Number	FDA Submission Document Number *(if known)*
(b) (4) [redacted]		

SECTION A TYPE OF SUBMISSION

PMA	PMA & HDE Supplement	PDP	510(k)	Meeting
☐ Original Submission	☐ Regular (180 day)	☐ Original PDP	☒ Original Submission:	☐ Pre-510(K) Meeting
☐ Premarket Report	☐ Special	☐ Notice of Completion	☒ Traditional	☐ Pre-IDE Meeting
☐ Modular Submission	☐ Panel Track (PMA Only)	☐ Amendment to PDP	☐ Special	☐ Pre-PMA Meeting
☐ Amendment	☐ 30-day Supplement		☐ Abbreviated (Complete section I, Page 5)	☐ Pre-PDP Meeting
☐ Report	☐ 30-day Notice		☐ Additional Information	☐ Day 100 Meeting
☐ Report Amendment	☐ 135-day Supplement		☐ Third Party	☐ Agreement Meeting
☐ Licensing Agreement	☐ Real-time Review			☐ Determination Meeting
	☐ Amendment to PMA & HDE Supplement			☐ Other *(specify):*
	☐ Other			

IDE	Humanitarian Device Exemption (HDE)	Class II Exemption Petition	Evaluation of Automatic Class III Designation (De Novo)	Other Submission
☐ Original Submission	☐ Original Submission	☐ Original Submission	☐ Original Submission	☐ 513(g)
☐ Amendment	☐ Amendment	☐ Additional Information	☐ Additional Information	☐ Other *(describe submission):*
☐ Supplement	☐ Supplement			
	☐ Report			
	☐ Report Amendment			

Have you used or cited Standards in your submission? ☒ Yes ☐ No *(If Yes, please complete Section I, Page 5)*

SECTION B SUBMITTER, APPLICANT OR SPONSOR

Company / Institution Name	Establishment Registration Number *(if known)*		
Covidien llc	3004962788		
Division Name *(if applicable)*	**Phone Number *(including area code)***		
Interventional Lung Solutions, formerly superDimension Inc.	763-210-4091		
Street Address	**FAX Number *(including area code)***		
161 Cheshire Lane Suite 100	763-210-4098		
City	**State / Province**	**ZIP/Postal Code**	**Country**
Minneapolis	MN	55441	U.S.A.
Contact Name			
Deborah Fleetham			
Contact Title	**Contact E-mail Address**		
Manager Regulatory Affairs	deborah.fleetham@covidien.com		

SECTION C APPLICATION CORRESPONDENT (e.g., consultant, if different from above)

Company / Institution Name			
Division Name *(if applicable)*	**Phone Number *(including area code)***		
	763-210-4062		
Street Address	**FAX Number *(including area code)***		
161 Cheshire Lane Suite 100	763-210-4098		
City	**State / Province**	**ZIP Code**	**Country**
Minneapolis	MN	55441	U.S.A.
Contact Name			
Kristen Swanson			
Contact Title	**Contact E-mail Address**		
Regulatory Consultant	kristen.swanson@covidien.com		

SECTION D1 REASON FOR APPLICATION - PMA, PDP, OR HDE

- ☐ New Device
- ☐ Withdrawal
- ☐ Additional or Expanded Indications
- ☐ Request for Extension
- ☐ Post-approval Study Protocol
- ☐ Request for Applicant Hold
- ☐ Request for Removal of Applicant Hold
- ☐ Request to Remove or Add Manufacturing Site

- ☐ Change in design, component, or specification:
  - ☐ Software / Hardware
  - ☐ Color Additive
  - ☐ Material
  - ☐ Specifications
  - ☐ Other *(specify below)*

- ☐ Location change:
  - ☐ Manufacturer
  - ☐ Sterilizer
  - ☐ Packager

- ☐ Process change:
  - ☐ Manufacturing ☐ Packaging
  - ☐ Sterilization
  - ☐ Other *(specify below)*

- ☐ Labeling change:
  - ☐ Indications
  - ☐ Instructions
  - ☐ Performance Characteristics
  - ☐ Shelf Life
  - ☐ Trade Name
  - ☐ Other *(specify below)*

- ☐ Report Submission:
  - ☐ Annual or Periodic
  - ☐ Post-approval Study
  - ☐ Adverse Reaction
  - ☐ Device Defect
  - ☐ Amendment

- ☐ Response to FDA correspondence:

- ☐ Change in Ownership
- ☐ Change in Correspondent
- ☐ Change of Applicant Address

- ☐ Other Reason *(specify):*

SECTION D2 REASON FOR APPLICATION - IDE

- ☐ New Device
- ☐ New Indication
- ☐ Addition of Institution
- ☐ Expansion / Extension of Study
- ☐ IRB Certification
- ☐ Termination of Study
- ☐ Withdrawal of Application
- ☐ Unanticipated Adverse Effect
- ☐ Notification of Emergency Use
- ☐ Compassionate Use Request
- ☐ Treatment IDE
- ☐ Continued Access

- ☐ Change in:
  - ☐ Correspondent / Applicant
  - ☐ Design / Device
  - ☐ Informed Consent
  - ☐ Manufacturer
  - ☐ Manufacturing Process
  - ☐ Protocol - Feasibility
  - ☐ Protocol - Other
  - ☐ Sponsor

- ☐ Report submission:
  - ☐ Current Investigator
  - ☐ Annual Progress Report
  - ☐ Site Waiver Report
  - ☐ Final

- ☐ Response to FDA Letter Concerning:
  - ☐ Conditional Approval
  - ☐ Deemed Approved
  - ☐ Deficient Final Report
  - ☐ Deficient Progress Report
  - ☐ Deficient Investigator Report
  - ☐ Disapproval
  - ☐ Request Extension of Time to Respond to FDA
  - ☐ Request Meeting
  - ☐ Request Hearing

- ☐ Other Reason *(specify):*

SECTION D3 REASON FOR SUBMISSION - 510(k)

- ☒ New Device
- ☐ Additional or Expanded Indications
- ☐ Change in Technology

- ☐ Other Reason *(specify):*

SECTION E ADDITIONAL INFORMATION ON 510(K) SUBMISSIONS

Product codes of devices to which substantial equivalence is claimed

1	KOG	2	EOQ	3		4	
5		6		7		8	

Summary of, or statement concerning, safety and effectiveness information

☒ 510 (k) summary attached
☐ 510 (k) statement

Information on devices to which substantial equivalence is claimed *(if known)*

	510(k) Number		*Trade or Proprietary or Model Name*		*Manufacturer*
1	K834402	1	Gastrointestinal Sheath Brush	1	Hobbs Medical
2	K944650	2	Wang Bronchial Needle Brush	2	ConMed Corporation
3		3		3	
4		4		4	
5		5		5	
6		6		6	

SECTION F PRODUCT INFORMATION - APPLICATION TO ALL APPLICATIONS

Common or usual name or classification name

Cytology Brush

	Trade or Proprietary or Model Name for This Device		Model Number
1	superTrax Triple-Needle Tipped Cytology Brush	1	SDTNB1000
2	superTrax Triple-Needle Tipped Cytology Brush	2	SDTNB1500
3		3	
4		4	
5		5	

FDA document numbers of all prior related submissions *(regardless of outcome)*

1	2	3	4	5	6
7	8	9	10	11	12

Data Included in Submission

☐ Laboratory Testing ☐ Animal Trials ☐ Human Trials

SECTION G PRODUCT CLASSIFICATION - APPLICATION TO ALL APPLICATIONS

Product Code	C.F.R. Section *(if applicable)*	Device Class
BTG	874.4680	☐ Class I ☒ Class II ☐ Class III ☐ Unclassified

Classification Panel

Ear, Nose, and Throat

Indications *(from labeling)*

To be utilized by physician / trained personnel through a flexible endoscope or the superDimension system for retrieving specimens from endobronchial lesions, peripheral lung nodules or lung masses.

Note: Submission of the information entered in Section H does not affect the need to submit device establishment registration.	FDA Document Number *(if known)*

SECTION H — MANUFACTURING / PACKAGING / STERILIZATION SITES RELATING TO A SUBMISSION

☒ Original ☐ Add ☐ Delete	Facility Establishment Identifier (FEI) Number: 1220592	☐ Manufacturer ☐ Contract Sterilizer ☒ Contract Manufacturer ☐ Repackager / Relabeler
Company / Institution Name		Establishment Registration Number
(b) (4) [redacted]		

☒ Original ☐ Add ☐ Delete	Facility Establishment Identifier (FEI) Number: 2246552	☐ Manufacturer ☒ Contract Sterilizer ☐ Contract Manufacturer ☐ Repackager / Relabeler
(b) (4) [redacted]		

☒ Original ☐ Add ☐ Delete	Facility Establishment Identifier (FEI) Number: 3004962788	☒ Manufacturer ☐ Contract Sterilizer ☐ Contract Manufacturer ☐ Repackager / Relabeler	
Company / Institution Name: Covidien llc		Establishment Registration Number: 3004962788	
Division Name *(if applicable)*: Interventional Lung Solutions		Phone Number *(including area code)*: 763-210-4062	
Street Address: 161 Cheshire Lane Suite 100		FAX Number *(including area code)*: 763-210-4098	
City: Minneapolis	State / Province: MN	ZIP Code: 55441	Country: U.S.A.
Contact Name: Kristen Swanson	Contact Title: Regulatory Consultant	Contact E-mail Address: kristen.swanson@covidien.com	

SECTION I — UTILIZATION OF STANDARDS

Note: Complete this section if your application or submission cites standards or includes a *"Declaration of Conformity to a Recognized Standard"* statement.

	Standards No.	Standards Organization	Standards Title	Version	Date
1	10993-1	ISO	Biological Evaluation of medical devices - Part 1: Evaluation and testing within a risk management proce	2009	15 Oct 2009
2	14971	ISO	Medical Devices - Application of Risk Management	2007 (R 2010)	05 Dec 2006
3	11135-1	ANSI/AAMI/ISO	Sterilization of health care products - Ethylene Oxide - Part 1: Requirements for development, validation, and routine control of a sterilization process for medical devices	2007	04 June 2007
4	F2096-11	ASTM	Standard Test Method for Detecting Gross Leaks in Packaging by Internal Pressurization Test (Bubble Test)	2011	01 Jan 2011
5	10993-5	ISO	Biological Evaluation of Medical Devices Part 5: Tests for in vitro Cytotoxicity	2009	01 Jun 2009
6	10993-7	ISO	Biological Evaluation of Medical Devices Part 7: Ethylene Oxide Sterilization Residuals	2008	10 Dec 2008
7	10993-10	ISO	Biological Evaluation of Medical Devices Part 10: Tests for irritation and skin sensitization	2010	04 Sep 2010

Please include any additional standards to be cited on a separate page.

Section I Utilization of Standards (Continued)					
8	Standards Number	Standards Organization	Standards Title	Version	Date
	F88/F88M-09	ASTM	Standard Test Method for Seal Strength of Flexible Barrier Materials	2009	15 Jun 2009

COVIDIEN

February 12, 2013

Food and Drug Administration
Center for Devices and Radiological Health
Document Mail Center
10903 New Hampshire Ave. Bldg 66 room G609
Silver Spring, MD 20993-0002

Re: 510(k) Notification for the superTrax® Triple-Needle tipped Cytology Brush

Attention: Document Mail Clerk

This Traditional 510(k) is being submitted to notify you of the intention of Covidien llc, formerly registered as superDimension Inc. (the 510(k) Applicant) to introduce a new Cytology Brush for use in bronchial applications. This cytology brush is substantially equivalent to existing products on the market except that instead of a single brush on the distal end, there are three smaller brushes. The information below provides the basic identity of the product and applicant.

Common name:	Bronchial Biopsy Brush
Proprietary Name:	superTrax® Triple Needle-Tipped Cytology Brush
Classification:	Class II – CFR 874.4680
Classification Name:	Brush, Biopsy, Bronchoscope (non-rigid)
Product Code:	BTG
Manufactured At:	Covidien llc, formerly registered as superDimension Inc.

Establishment Registration Number: 3004962788

There are no applicable special controls for this device.

In addition to the required sections of the 510(k), an additional section, Desired Claims, has been added to document the claims that Covidien llc would like to use in marketing literature.

This paper copy is accompanied by an eCopy which is an exact duplicate of the paper copy.

510(k) Applicant:
Deborah Fleetham
Manager, Regulatory Affairs
Covidien llc
161 Cheshire Lane, Suite 100
Minneapolis, MN 55441

Please direct all questions or correspondence to the 510(k) Application Correspondent listed below.

510(k) Application Correspondent:
Kristen Swanson
Regulatory Affairs Consultant
Prepared for Covidien llc
161 Cheshire Lane, Suite 100
Minneapolis, MN 55441
Phone: 763-210-4062
Fax: 763-210-4098
Email: kristen.swanson@covidien.com

Sincerely,

Deborah Fleetham

Deborah Fleetham
Manager, Regulatory Affairs
Phone: 763-210-4091
Fax: 763-210-4098
Email: deborah.fleetham@covidien.com

510(k) Screening Checklist

Title	Related Information	Present	Inadequate	N/A
MDUFMA Cover Sheet	Medical Device User Fee Cover Sheet[3]	✓		
CDRH Premarket Review Submission Cover Sheet	CDRH Premarket Review Submission Cover Sheet[4]	✓		
510(k) Cover Letter	Appendix A of "Guidance for Industry and FDA Staff Format for Traditional and Abbreviated 510(k)s" updated November 17, 2005	✓		
Indications for Use Statement	Device Advice "Content of a 510(k)" Section D[5]	✓		
510(k) Summary or 510(k) Statement	Device Advice "Content of a 510(k)" Section E[6]	✓		
Truthful and Accuracy Statement	Device Advice "Content of a 510(k)" Section G[7]	✓		
Class III Summary and Certification	Class III Summary and Certification Form[8]			✓
Financial Certification or Disclosure Statement	FORM FDA 3454, Certification: Financial Interests and Arrangements of Clinical Investigators[9] FORM FDA 3455, Disclosure: Financial Interests and Arrangements of Clinical Investigators[10] Financial Disclosure by Clinical Investigators[11]			✓
Declarations of Conformity and Summary Reports (Abbreviated 510(k)s)	Use of Standards in Substantial Equivalence Determinations[12] FDA Standards program[13] Declaration of conformity[14] Required Elements for Declaration of Conformity to Recognized Standard[15]			✓
Executive Summary	See section 10 in Chapter II of "Guidance for Industry and FDA Staff Format for Traditional and Abbreviated 510(k)s" updated November 17, 2005	✓		
Device Description	See section 11 in Chapter II of "Guidance for Industry and FDA Staff Format for Traditional and Abbreviated 510(k)s" updated November 17, 2005	✓		
Substantial Equivalence Discussion	Guidance on the CDRH Premarket Notification Review Program 6/30/86 (K86-3)[16]	✓		
Proposed Labeling	Device Advice " Content of a 510(k)" Section H[17]	✓		

Sterilization/Shelf Life	Updated 510(k) Sterility Review Guidance (K90-1)[18] For reuse of single use devices, see Guidance for Industry and FDA Staff – Medical Device User Fee and Modernization Act of 2002 Validation Data in Premarket Notification Submissions (510(k)s) for Reprocessed Single-Use Medical Devices[19]	✓		
Biocompatibility	FDA Blue Book Memo, G95-1, Use of International Standard ISO-10993, "Biological Evaluation of Medical Devices Part 1: Evaluation and Testing"[20]	✓		
Software	Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices[21]			✓
Electromagnetic Compatibility/Electrical Safety	CDRH Medical Device Electromagnetic Compatibility Program[22] See also IEC 60601-1- 2 Medical Electrical Equipment -- Part 1: General Requirements for Safety; Electromagnetic Compatibility -- Requirements and Tests (Second Edition, 2001)			✓
Performance Testing – Bench	See section 18 in Chapter II of "Guidance for Industry and FDA Staff Format for Traditional and Abbreviated 510(k)s" updated November 17, 2005	✓		
Performance Testing – Animal	See section 19 in Chapter II of "Guidance for Industry and FDA Staff Format for Traditional and Abbreviated 510(k)s" updated November 17, 2005			✓
Performance Testing – Clinical	See section 20 in Chapter II of "Guidance for Industry and FDA Staff Format for Traditional and Abbreviated 510(k)s" updated November 17, 2005 FORM FDA 3454, Certification: Financial Interests and Arrangements of Clinical Investigators[23] FORM FDA 3455, Disclosure: Financial Interests and Arrangements of Clinical Investigators[24]			✓

FORM FDA 3654, Standards Data Report for 510(k)s[25]	Standards Data Report Form – Form 3654 1. No standard used - No Standards Form Required 2. Declaration of Conformity – Yes Standards Form Required 3. Standard but no declaration – Yes Standards Form Required	✓		
Kit Certification	Device Advice[26]			✓

Table of Contents

List of Attachments

Attachment 9 – Biocompatibility Testing – DBR00015
Attachment 10 – Design Verification Testing –Protocols DVT00177 and DVT00189 and Reports DVR000188 and DVR00194

Section 1 Indications for Use

The Indications for Use are included on the following page.

Indications for Use

510(k) Number (if known):

Device Name: superDimension® superTrax® Triple Needle-Tipped Cytology Brush

Indications for Use:

To be utilized by physician / trained personnel through a flexible endoscope or the superDimension system for retrieving specimens from endobronchial lesions, peripheral lung nodules or lung masses.

Prescription Use _X_ AND / OR Over-the-Counter Use _____
(Part 21 CFR 801 Subpart D) (21 CFR 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE – CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

Section 2 510(k) Summary

The 510(k) Summary is included on the following page.

510(k) Summary
Covidien llc
Traditional 510(k)
superTrax® Triple Needle-Tipped Cytology Brush

Date Prepared:

2/11/2013

510(k) Applicant:
Deborah Fleetham
Manager Regulatory Affairs
Covidien llc, formerly registered as superDimension Inc.
161 Cheshire Lane Suite 100
Minneapolis, MN 55441 U.S.A.
Ph: 763-210-4091
Fax: 763-210-4098
Email : deborah.fleetham@covidien.com

Name of Device :

Trade Name :	superTrax® Triple Needle-Tipped Cytology Brush
Common Name:	Bronchial Biopsy Brush
Classification Name:	Brush, Biopsy, Bronchoscope (non-rigid) 21 CFR Part 874.4680
Product code:	BTG

Equivalent Legally-Marketed Device:

K834402 Gastrointestinal Sheath Brush (KOG) by Hobbs Medical, Inc.

K944650 Wang Bronchial Needle Brush (EOQ) by ConMed

Description:
The superTrax® Triple Needle-Tipped Cytology Brush is designed for use with standard bronchoscopes or with the superDimension system. The superTrax® Triple Needle-Tipped Cytology Brush is designed to provide high specimen yield and ease of use. This device features Ethylene Tetrafluoroethylene (ETFE) sheathing and sharpened tips that can be used to rough up tissue to obtain a sample of tissue/cells. The superTrax triple needle-tipped brush is similar to currently marketed cytology brushes except that it has three smaller brushes in place of one larger brush.

Intended Use:
To be utilized by physician / trained personnel through a flexible endoscope or the superDimension system for retrieving specimens from endobronchial lesions, peripheral lung nodules or lung masses.

Summary of Characteristics Compared to Predicate Device:
The use of the superTrax® Triple Needle-Tipped Cytology Brush is equivalent to the predicate devices in that these devices are all advanced into the body either individually or through a separate catheter channel. Once they reach the target biopsy site, a sample is taken from the desired site. While the predicate devices each contain one larger brush, the superTrax® Triple Needle-Tipped Cytology Brush contains three smaller brushes. Once the sample is obtained, the brushes are retracted back into the sheath and the entire tool is withdrawn from the body.

The superTrax Triple Needle-tipped Cytology brush and the predicate devices are all single use, sterile devices. The shaft length, materials, and function are substantially similar with the same technological function.

Performance Data:
In-vitro testing has been performed and all components, subassemblies, and /or full devices met the required specifications for the completed tests.

Clinical Data:
Clinical tests were not required to validate the design of the superTrax® Triple Needle-Tipped Cytology Brush due to the extensive history of similar devices.

Conclusion:
Covidien llc has demonstrated that the proposed superTrax® Triple Needle-Tipped Cytology Brush is substantially equivalent to Gastrointestinal Sheath Brush (KOG) by Hobbs Medical, Inc. K834402, and the Wang Bronchial Needle Brush (EOQ) by ConMed K944650.

Section 3 Truthful and Accuracy Statement

The Premarket Notification Truthful and Accurate Statement is included on the following page.

Premarket Notification Truthful And Accurate Statement

[As Required by 21 CFR 807.87(k)]

I certify that, in my capacity as Manager of Regulatory Affairs of Covidien llc., I believe to the best of my knowledge, that all data and information submitted in the premarket notification are truthful and accurate and that no material fact has been omitted.

Deborah Fleetham

(Date)

11 Feb 2013

*(Premarket Notification [510(k)] Number)

*For a new submission, leave the 510(k) number blank.

Must be signed by a responsible person of the firm required to submit the premarket notification [e.g., not a consultant for the 510(k) submitter].

Section 4 Class III Summary and Certification

This device is a Class II device therefore this section is not applicable.

Section 5 Financial Certification or Disclosure Statement

Since no clinical trials are included as part of this submission, this section is not applicable.

Section 6 Declarations of Conformity and Summary Reports

Testing of the superTrax Triple Needle-Tipped Cytology Brush utilized recognized standards wherever possible. Specific testing results are discussed in the relevant sections of this submission. This submission declares conformity to the following standards and has included copies of the Standards Data Report for 510(k)s, FDA form 3654 for each one.

AAMI / ANSI/ ISO 11135-1: 2007 Sterilization of Health Care Products – Ethylene Oxide Part 1: Requirements for the development, validation, and routine control of a sterilization process for medical devices

AAMI / ANSI / ISO 10993-1: 2009 Biological evaluation of medical devices Part 1: Evaluation and testing within a risk management process

AAMI / ANSI / ISO 10993-5:2009 Biological Evaluation of Medical Devices Part 5: Tests for in Vitro Cytotoxicity

AAMI / ANSI / ISO 10993-7:2008 Biological Evaluation of Medical Devices Part 7: Ethylene oxide Sterilization Residuals

ISO 10993-10:2010 Biological Evaluation of Medical Devices Part 10: Tests for irritation and skin sensitization

AAMI / ANSI/ISO 14971: 2007 (R)2010 Medical Devices – Applications of risk management to medical devices

ASTM F2096-11 Standard Test method for Detecting Gross Leaks in Packaging by Internal Pressurization (Bubble Test)

ASTM F88/F88M-09 Standard Test Method for Seal Strength of Flexible Barrier Materials

Form Approved: OMB No. 0910-0120; Expiration Date: 12/31/13

Department of Health and Human Services
Food and Drug Administration

STANDARDS DATA REPORT FOR 510(k)s

(To be filled in by applicant)

This report and the Summary Report Table are to be completed by the applicant when submitting a 510(k) that references a national or international standard. A separate report is required for each standard referenced in the 510(k).

TYPE OF 510(K) SUBMISSION

☒ Traditional ☐ Special ☐ Abbreviated

STANDARD TITLE [1]

AAMI / ANSI / ISO 11135-1:2007, Sterilization of health care products - Ethylene oxide - Part 1: Requirements for the developmen

Please answer the following questions	Yes	No
Is this standard recognized by FDA [2]?	☒	☐
FDA Recognition number [3]	# 14-228	
Was a third party laboratory responsible for testing conformity of the device to this standard identified in the 510(k)?	☒	☐
Is a summary report [4] describing the extent of conformance of the standard used included in the 510(k)? If no, complete a summary report table.	☒	☐
Does the test data for this device demonstrate conformity to the requirements of this standard as it pertains to this device?	☒	☐
Does this standard include acceptance criteria? If no, include the results of testing in the 510(k).	☒	☐
Does this standard include more than one option or selection of tests? If yes, report options selected in the summary report table.	☐	☒
Were there any deviations or adaptations made in the use of the standard?	☐	☒
If yes, were deviations in accordance with the FDA supplemental information sheet (SIS) [5]?	☐	☐
Were deviations or adaptations made beyond what is specified in the FDA SIS? If yes, report these deviations or adaptations in the summary report table.	☐	☒
Were there any exclusions from the standard? If yes, report these exclusions in the summary report table.	☐	☒
Is there an FDA guidance [6] that is associated with this standard?	☐	☒
If yes, was the guidance document followed in preparation of this 510k?	☐	☒

Title of guidance: _____

[1] The formatting convention for the title is: [SDO] [numeric identifier] [title of standard] [date of publication]

[2] Authority [21 U.S.C. 360d], www.fda.gov/cdrh/stdsprog.html

[3] http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm

[4] The summary report should include: any adaptations used to adapt to the device under review (for example, alternative test methods); choices made when options or a selection of methods are described; deviations from the standard; requirements not applicable to the device; and the name and address of the test laboratory or certification body involved in conformance assessment to this standard. The summary report includes information on all standards utilized during the development of the device.

[5] The supplemental information sheet (SIS) is additional information which is necessary before FDA recognizes the standard. Found at http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm

[6] The online search for CDRH Guidance Documents can be found at www.fda.gov/cdrh/guidance.html

PSC Graphics (301) 443-6740 EF

EXTENT OF STANDARD CONFORMANCE
SUMMARY REPORT TABLE

STANDARD TITLE
AAMI / ANSI / ISO 11135-1:2007, Sterilization of health care products - Ethylene oxide - Part 1: Requirements for the developmen

CONFORMANCE WITH STANDARD SECTIONS*

SECTION NUMBER	SECTION TITLE	CONFORMANCE? ☐ Yes ☐ No ☐ N/A
TYPE OF DEVIATION OR OPTION SELECTED ◆		
DESCRIPTION		
JUSTIFICATION		
SECTION NUMBER	SECTION TITLE	CONFORMANCE? ☐ Yes ☐ No ☐ N/A
TYPE OF DEVIATION OR OPTION SELECTED ◆		
DESCRIPTION		
JUSTIFICATION		
SECTION NUMBER	SECTION TITLE	CONFORMANCE? ☐ Yes ☐ No ☐ N/A
TYPE OF DEVIATION OR OPTION SELECTED ◆		
DESCRIPTION		
JUSTIFICATION		

* For completeness list all sections of the standard and indicate whether conformance is met. If a section is not applicable (N/A) an explanation is needed under "justification." Some standards include options, so similar to deviations, the option chosen needs to be described and adequately justified as appropriate for the subject device. Explanation of all deviations or description of options selected when following a standard is required under "type of deviation or option selected," "description" and "justification" on the report. More than one page may be necessary.

◆ Types of deviations can include an exclusion of a section in the standard, a deviation brought out by the FDA supplemental information sheet (SIS), a deviation to adapt the standard to the device, or any adaptation of a section.

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Department of Health and Human Services
Food and Drug Administration

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TYPE OF 510(K) SUBMISSION

☒ Traditional ☐ Special ☐ Abbreviated

STANDARD TITLE [1]

AAMI / ANSI / ISO 14971:2007 (R)2010 Medical devices - Applications of risk management to medical devices

Please answer the following questions	Yes	No
Is this standard recognized by FDA [2]?	☒	☐
FDA Recognition number [3]	# 5-70	
Was a third party laboratory responsible for testing conformity of the device to this standard identified in the 510(k)?	☐	☒
Is a summary report [4] describing the extent of conformance of the standard used included in the 510(k)? If no, complete a summary report table.	☒	☐
Does the test data for this device demonstrate conformity to the requirements of this standard as it pertains to this device?	☒	☐
Does this standard include acceptance criteria? If no, include the results of testing in the 510(k).	☐	☒
Does this standard include more than one option or selection of tests? If yes, report options selected in the summary report table.	☐	☒
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If yes, was the guidance document followed in preparation of this 510k?	☐	☐

Title of guidance: _____

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EXTENT OF STANDARD CONFORMANCE
SUMMARY REPORT TABLE

STANDARD TITLE
AAMI / ANSI / ISO 14971:2007 (R)2010 Medical devices - Applications of risk management to medical devices

CONFORMANCE WITH STANDARD SECTIONS*

SECTION NUMBER	SECTION TITLE	CONFORMANCE? ☐ Yes ☐ No ☐ N/A
TYPE OF DEVIATION OR OPTION SELECTED ◆		
DESCRIPTION		
JUSTIFICATION		

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Paperwork Reduction Act Statement

Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Department of Health and Human Services
Food and Drug Administration
Office of Chief Information Officer
1350 Piccard Drive, Room 400
Rockville, MD 20850

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

Form Approved: OMB No. 0910-0120; Expiration Date: 12/31/13

Department of Health and Human Services
Food and Drug Administration

STANDARDS DATA REPORT FOR 510(k)s

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TYPE OF 510(K) SUBMISSION

☒ Traditional ☐ Special ☐ Abbreviated

STANDARD TITLE [1]

AAMI / ANSI / ISO 10993-1:2009 Biological evaluation of medical devices Part 1: Evaluation and testing within a risk managemen

Please answer the following questions	Yes	No
Is this standard recognized by FDA [2]?	☒	☐
FDA Recognition number [3]	# 2-156	
Was a third party laboratory responsible for testing conformity of the device to this standard identified in the 510(k)?	☐	☒
Is a summary report [4] describing the extent of conformance of the standard used included in the 510(k)? If no, complete a summary report table.	☒	☐
Does the test data for this device demonstrate conformity to the requirements of this standard as it pertains to this device?	☒	☐
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If yes, was the guidance document followed in preparation of this 510k?	☒	☐

Title of guidance: Bluebook Memorandum G95-1 "Use of Internationals Standard ISO 10993

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[2] Authority [21 U.S.C. 360d], www.fda.gov/cdrh/stdsprog.html

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STANDARD TITLE
AAMI / ANSI / ISO 10993-1:2009 Biological evaluation of medical devices Part 1: Evaluation and testing within a risk managemen

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TYPE OF DEVIATION OR OPTION SELECTED ◆		
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Department of Health and Human Services
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1350 Piccard Drive, Room 400
Rockville, MD 20850

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Form Approved: OMB No. 0910-0120; Expiration Date: 12/31/13

Department of Health and Human Services
Food and Drug Administration

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TYPE OF 510(K) SUBMISSION

☒ Traditional ☐ Special ☐ Abbreviated

STANDARD TITLE [1]

AAMI / ANSI / ISO 10993-5:2009 Biological Evaluation of Medical Devices Part 5: Tests for in Vitro Cytotoxicity

Please answer the following questions	Yes	No
Is this standard recognized by FDA [2] ?	☒	☐
FDA Recognition number [3]	# 2-153	
Was a third party laboratory responsible for testing conformity of the device to this standard identified in the 510(k)?	☒	☐
Is a summary report [4] describing the extent of conformance of the standard used included in the 510(k)? If no, complete a summary report table.	☒	☐
Does the test data for this device demonstrate conformity to the requirements of this standard as it pertains to this device?	☒	☐
Does this standard include acceptance criteria? If no, include the results of testing in the 510(k).	☐	☒
Does this standard include more than one option or selection of tests? If yes, report options selected in the summary report table.	☒	☐
Were there any deviations or adaptations made in the use of the standard?	☐	☒
If yes, were deviations in accordance with the FDA supplemental information sheet (SIS) [5] ?	☐	☐
Were deviations or adaptations made beyond what is specified in the FDA SIS? If yes, report these deviations or adaptations in the summary report table.	☐	☒
Were there any exclusions from the standard? If yes, report these exclusions in the summary report table.	☐	☒
Is there an FDA guidance [6] that is associated with this standard?	☒	☐
If yes, was the guidance document followed in preparation of this 510k?	☒	☐

Title of guidance: Bluebook Memorandum G95-1 "Use of Internationals Standard ISO 10993

[1] The formatting convention for the title is: [SDO] [numeric identifier] [title of standard] [date of publication]

[2] Authority [21 U.S.C. 360d], www.fda.gov/cdrh/stdsprog.html

[3] http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm

[4] The summary report should include: any adaptations used to adapt to the device under review (for example, alternative test methods); choices made when options or a selection of methods are described; deviations from the standard; requirements not applicable to the device; and the name and address of the test laboratory or certification body involved in conformance assessment to this standard. The summary report includes information on all standards utilized during the development of the device.

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[6] The online search for CDRH Guidance Documents can be found at www.fda.gov/cdrh/guidance.html

EXTENT OF STANDARD CONFORMANCE
SUMMARY REPORT TABLE

STANDARD TITLE
AAMI / ANSI / ISO 10993-5:2009 Biological Evaluation of Medical Devices Part 5: Tests for in Vitro Cytotoxicity

CONFORMANCE WITH STANDARD SECTIONS*

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
4	Sample and control Preparation	☒ Yes ☐ No ☐ N/A

TYPE OF DEVIATION OR OPTION SELECTED ◆
Used extraction method

DESCRIPTION
Method described in 510(k) and attached report

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
		☐ Yes ☐ No ☐ N/A

TYPE OF DEVIATION OR OPTION SELECTED ◆

DESCRIPTION

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
		☐ Yes ☐ No ☐ N/A

TYPE OF DEVIATION OR OPTION SELECTED ◆

DESCRIPTION

JUSTIFICATION

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STANDARDS DATA REPORT FOR 510(k)s

(To be filled in by applicant)

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TYPE OF 510(K) SUBMISSION

☒ Traditional ☐ Special ☐ Abbreviated

STANDARD TITLE [1]

AAMI / ANSI / ISO 10993-7: 2008 Biological Evaluation of Medical Devices Part 7: Ethylene Oxide Sterilization Residuals

Please answer the following questions	Yes	No
Is this standard recognized by FDA [2]?	☒	☐
FDA Recognition number [3]	# 14-278	
Was a third party laboratory responsible for testing conformity of the device to this standard identified in the 510(k)?	☒	☐
Is a summary report [4] describing the extent of conformance of the standard used included in the 510(k)? If no, complete a summary report table.	☒	☐
Does the test data for this device demonstrate conformity to the requirements of this standard as it pertains to this device?	☒	☐
Does this standard include acceptance criteria? If no, include the results of testing in the 510(k).	☒	☐
Does this standard include more than one option or selection of tests? If yes, report options selected in the summary report table.	☐	☒
Were there any deviations or adaptations made in the use of the standard?	☐	☒
If yes, were deviations in accordance with the FDA supplemental information sheet (SIS) [5]?	☐	☐
Were deviations or adaptations made beyond what is specified in the FDA SIS? If yes, report these deviations or adaptations in the summary report table.	☐	☒
Were there any exclusions from the standard? If yes, report these exclusions in the summary report table.	☐	☒
Is there an FDA guidance [6] that is associated with this standard?	☐	☒
If yes, was the guidance document followed in preparation of this 510k?	☐	☐

Title of guidance: _____

[1] The formatting convention for the title is: [SDO] [numeric identifier] [title of standard] [date of publication]

[2] Authority [21 U.S.C. 360d], www.fda.gov/cdrh/stdsprog.html

[3] http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm

[4] The summary report should include: any adaptations used to adapt to the device under review (for example, alternative test methods); choices made when options or a selection of methods are described; deviations from the standard; requirements not applicable to the device; and the name and address of the test laboratory or certification body involved in conformance assessment to this standard. The summary report includes information on all standards utilized during the development of the device.

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[6] The online search for CDRH Guidance Documents can be found at www.fda.gov/cdrh/guidance.html

EXTENT OF STANDARD CONFORMANCE
SUMMARY REPORT TABLE

STANDARD TITLE
AAMI / ANSI / ISO 10993-7:2008 Biological Evaluation of Medical Devices Part 7: Ethylene Oxide Sterilization Residuals

CONFORMANCE WITH STANDARD SECTIONS*

SECTION NUMBER	SECTION TITLE	CONFORMANCE? ☐ Yes ☐ No ☐ N/A
TYPE OF DEVIATION OR OPTION SELECTED ❖		
DESCRIPTION		
JUSTIFICATION		

SECTION NUMBER	SECTION TITLE	CONFORMANCE? ☐ Yes ☐ No ☐ N/A
TYPE OF DEVIATION OR OPTION SELECTED ❖		
DESCRIPTION		
JUSTIFICATION		

SECTION NUMBER	SECTION TITLE	CONFORMANCE? ☐ Yes ☐ No ☐ N/A
TYPE OF DEVIATION OR OPTION SELECTED ❖		
DESCRIPTION		
JUSTIFICATION		

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TYPE OF 510(K) SUBMISSION

☒ Traditional ☐ Special ☐ Abbreviated

STANDARD TITLE [1]

ISO 10993-10: 2010 Biological Evaluation of Medical Devices Part 10: Tests for irritation and skin sensitization

Please answer the following questions	Yes	No
Is this standard recognized by FDA [2]?	☒	☐
FDA Recognition number [3]	# 2-174	
Was a third party laboratory responsible for testing conformity of the device to this standard identified in the 510(k)?	☒	☐
Is a summary report [4] describing the extent of conformance of the standard used included in the 510(k)? If no, complete a summary report table.	☒	☐
Does the test data for this device demonstrate conformity to the requirements of this standard as it pertains to this device?	☒	☐
Does this standard include acceptance criteria? If no, include the results of testing in the 510(k).	☐	☒
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Were there any deviations or adaptations made in the use of the standard?	☐	☒
If yes, were deviations in accordance with the FDA supplemental information sheet (SIS) [5]?	☐	☐
Were deviations or adaptations made beyond what is specified in the FDA SIS? If yes, report these deviations or adaptations in the summary report table.	☐	☒
Were there any exclusions from the standard? If yes, report these exclusions in the summary report table.	☐	☒
Is there an FDA guidance [6] that is associated with this standard?	☒	☐
If yes, was the guidance document followed in preparation of this 510k?	☒	☐

Title of guidance: Bluebook Memorandum G95-1

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PSC Graphics (301) 443-6740 EF

EXTENT OF STANDARD CONFORMANCE
SUMMARY REPORT TABLE

STANDARD TITLE
ISO 10993-10: 2010 Biological Evaluation of Medical Devices Part 10: Tests for irritation and skin sensitization

CONFORMANCE WITH STANDARD SECTIONS*

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
Annex B5	Vaginal Irritation Tests	☒ Yes ☐ No ☐ N/A

TYPE OF DEVIATION OR OPTION SELECTED ◆
The vaginal irritation test was selected due to the similarity of this tissue compared to the lung.

DESCRIPTION

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
		☐ Yes ☐ No ☐ N/A

TYPE OF DEVIATION OR OPTION SELECTED ◆

DESCRIPTION

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
		☐ Yes ☐ No ☐ N/A

TYPE OF DEVIATION OR OPTION SELECTED ◆

DESCRIPTION

JUSTIFICATION

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TYPE OF 510(K) SUBMISSION

☒ Traditional ☐ Special ☐ Abbreviated

STANDARD TITLE [1]

ASTM F2096-11, Standard Test Method for Detecting Gross LEaks in Packaging by Internal Pressurization (Bubble Test)

Please answer the following questions	Yes	No
Is this standard recognized by FDA [2]?	☒	☐
FDA Recognition number [3] # 14-359		
Was a third party laboratory responsible for testing conformity of the device to this standard identified in the 510(k)?	☒	☐
Is a summary report [4] describing the extent of conformance of the standard used included in the 510(k)? If no, complete a summary report table.	☒	☐
Does the test data for this device demonstrate conformity to the requirements of this standard as it pertains to this device?	☒	☐
Does this standard include acceptance criteria? If no, include the results of testing in the 510(k).	☒	☐
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Title of guidance: _____

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EXTENT OF STANDARD CONFORMANCE
SUMMARY REPORT TABLE

STANDARD TITLE
ASTM F2096-11, Standard Test Method for Detecting Gross LEaks in Packaging by Internal Pressurization (Bubble Test)

CONFORMANCE WITH STANDARD SECTIONS*

SECTION NUMBER	SECTION TITLE	CONFORMANCE? ☐ Yes ☐ No ☐ N/A

TYPE OF DEVIATION OR OPTION SELECTED ❖

DESCRIPTION

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE? ☐ Yes ☐ No ☐ N/A

TYPE OF DEVIATION OR OPTION SELECTED ❖

DESCRIPTION

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE? ☐ Yes ☐ No ☐ N/A

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DESCRIPTION

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TYPE OF 510(K) SUBMISSION

☒ Traditional ☐ Special ☐ Abbreviated

STANDARD TITLE [1]

ASTM F88/F88M-09 Standard Test Method for Seal Strength of Flexible Barrier Materials

Please answer the following questions	Yes	No
Is this standard recognized by FDA [2]?	☒	☐
FDA Recognition number [3]	# 14-283	
Was a third party laboratory responsible for testing conformity of the device to this standard identified in the 510(k)?	☒	☐
Is a summary report [4] describing the extent of conformance of the standard used included in the 510(k)? If no, complete a summary report table.	☒	☐
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Is there an FDA guidance [6] that is associated with this standard?	☐	☒
If yes, was the guidance document followed in preparation of this 510k?	☐	☒

Title of guidance: _____

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EXTENT OF STANDARD CONFORMANCE
SUMMARY REPORT TABLE

STANDARD TITLE
ASTM F88/F88M-09 Standard Test Method for Seal Strength of Flexible Barrier Materials

CONFORMANCE WITH STANDARD SECTIONS*

SECTION NUMBER	SECTION TITLE	CONFORMANCE? ☐ Yes ☐ No ☐ N/A

TYPE OF DEVIATION OR OPTION SELECTED ❖

DESCRIPTION

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE? ☐ Yes ☐ No ☐ N/A

TYPE OF DEVIATION OR OPTION SELECTED ❖

DESCRIPTION

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE? ☐ Yes ☐ No ☐ N/A

TYPE OF DEVIATION OR OPTION SELECTED ❖

DESCRIPTION

JUSTIFICATION

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Section 7 Executive Summary

The superTrax® Triple Needle-Tipped Cytology Brush is designed for use with standard bronchoscopes or with the superDimension system. The superTrax® Triple Needle-Tipped Cytology Brush is intended to be utilized by physicians or trained personnel through a flexible endoscope or the superDimension system for retrieving specimens from endobronchial lesions, peripheral lung nodules or lung masses. It is designed to provide high specimen yield and ease of use. This device features sharpened tips on the brushes distal end that can be used to rough up tissue to obtain a sample of tissue or cells. The superTrax triple needle-tipped brush is substantially equivalent to the devices marketed under the following 510(k)s.

- K834402 Gastrointestinal Sheath Brush (KOG) by Hobbs Medical, Inc.
- K944650 Wang Bronchial Needle Brush (EOQ) by ConMed)

The use of the superTrax® Triple Needle-Tipped Cytology Brush is equivalent to the predicate devices in that these devices are all cytology brushes which are advanced into the body either individually or through a separate catheter channel. Once it reaches the target biopsy site, a tissue sample is taken from the desired site. While the predicate devices each contain one larger brush, the superTrax® Triple Needle-Tipped Cytology Brush contains three smaller brushes. Once the operator believes that the sample is obtained, the brushes are retracted back into the sheath and the entire tool is withdrawn from the body.

The superTrax Triple Needle-tipped Cytology brush and the predicate devices are all single use, sterile devices. The shaft length, materials, and function are substantially similar with the same technological function. A comparison of each devices' features is shown in the following table.

Table 1: Comparison between Predicate Devices and the superTrax Triple Needle-tipped Brush

Characteristic	**superTrax Triple Needle-Tipped Brush**	**Hobbs Cytology Brush K834402**	**ConMed Needle-Tip Cytology Brush K944650**
Indication for Use	To be utilized by physician / trained personnel through a flexible endoscope or the superDimension system for retrieving specimens	To be utilized by a trained physician and / or trained personnel through a flexible endoscope when brush cell samples	For retrieving cytology specimens from endobronchial lesions, peripheral lung nodules or lung masses using

Characteristic	superTrax Triple Needle-Tipped Brush	Hobbs Cytology Brush K834402	ConMed Needle-Tip Cytology Brush K944650
	from endobronchial lesions, peripheral lung nodules or lung masses.	are required for cytological analysis.	flexible bronchoscopes
Single / Multiple Use	Single Use	Single Use	Single Use
Contraindications	None	Those associated with Bronchoscopy and GI Endoscopy in gaining access to the desired site Uncooperative Patient	None
Aspiration Port	Yes	No	Yes
Supplied Sterile	Yes	Yes	Yes
Sterilization Technique	Ethylene Oxide	Ethylene Oxide	Ethylene Oxide
Retractable Brush	Yes	Yes	Yes
Retraction Mechanism	Thumb Ring	Thumb Ring	Luer Cap
Outer Sheath Material	ETFE	PTFE	Not Known
Outer Sheath Diameter	1.92 mm	1.70 mm	1.9 mm
Catheter Length	115 cm	120 cm	140 cm
Number of Brushes	Three	One	One
Brush Length	10 mm and 15 mm	13 mm	11 mm

Characteristic	superTrax Triple Needle-Tipped Brush	Hobbs Cytology Brush K834402	ConMed Needle-Tip Cytology Brush K944650
Brush Diameter	.85 mm	3.0 mm	1.7 mm
Sharpened Tips	Yes	No	Yes
Inner Wire Material	304 Stainless Steel	304 Stainless Steel	Not known
Shaft Markers	Present	None	None
Proximal Connector	Luer	Luer	Luer

Performance Data:
In addition to dimensional testing, fluroscopic, trackability, and kinkability testing were done on the predicate devices as well as the superTrax product. Results demonstrated substantially equivelent performance on these attributes.

This data demonstrates that the superTrax Triple Needle-Tipped Cytology Brush is substantially equivalent to the predicate devices based on materials, length, diameter, sterilization method, indication for use, and construction.

Section 8 Device Description

The superTrax Triple Needle-Tipped Brush is designed for use with the superDimension System. It is an endoscopic catheter comprised of an outer sheathing and an inner catheter assembly. The inner catheter assembly consists of a thumb ring at the proximal end and a twisted wire shaft to connect to the distal end. The distal end terminates in three connected brushes. The brushes have sharpened ends, referred to as needle-tipped, that can be used to rough up tissue to obtain a sample of tissue or cells.

There are two sets of markings on the proximal end of the shaft. One set of markings is labeled as EWC and is black while the other set of markings is labeled as EDGE EWC and is blue. As the proximal end of the catheter will not come in contact with the patient a Color Additive Petition is not applicable. EWC stands for Extended Working Channel. The EWC is a superDimension catheter used as part with the Electromagnetic Navigation Bronchoscopy system. The Edge EWC markers are located [redacted] from the distal end and 10 centimeters proximal to the EWC black markings which is [redacted] from the distal end. Each set of markings consists of a thicker, more distal mark followed by four additional marks [redacted] increments. The purpose of these marks is to allow the physician to position the distal end of the Triple Needle-Tipped Brush flush with the distal end of the specific EWC being used. The Edge EWC system is 10 cm longer than the standard EWC therefore requiring two separate sets of marks. A picture of the Triple Needle-Tipped Catheter shaft with the markings is shown in the figure below.

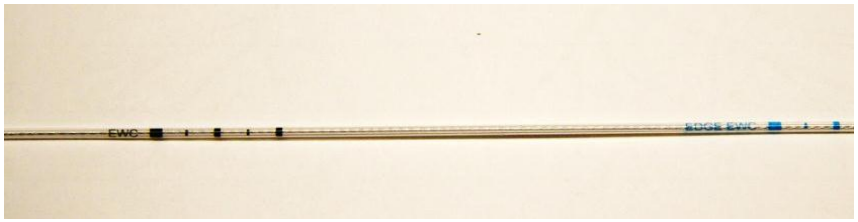

Figure 1: Close-up of Triple Needle-Tipped Brush Shaft Markings on proximal end

When the catheter is used, it is inserted into a channel such as a bronchoscope or superDimension Extended Working Channel (EWC) with the distal brush in a retracted position inside the outer sheath. This position is shown in Figure 2.

Figure 2: Distal Tip Retracted in the sheath

When the catheter is in position as indicated by the markings on the shaft, the brushes can be extended into the tissue to obtain tissue samples by advancing the proximal thumb ring which is shown in Figure 3 below.

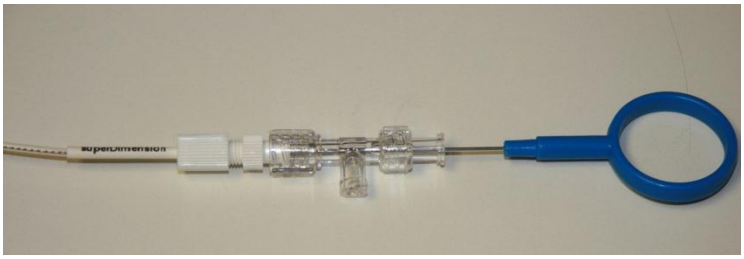

Figure 3: Proximal Thumb ring and aspirating port

Once the brushes are advanced out of the sheath, there is a slight flare to the brushes allowing them to potentially sample tissue from a larger area. The distal end is shown in Figure 4. If desired, the physician can use the aspiration port to obtain a slight vacuum to pull cells into the catheter. When the physician believes that an adequate sample has been taken, usually after several advances and withdrawals of the brushes, the brushes are retracted back into the sheath and then the entire catheter is withdrawn from the channel. Physicians then follow their standard practice to remove cells from the brushes and tool.

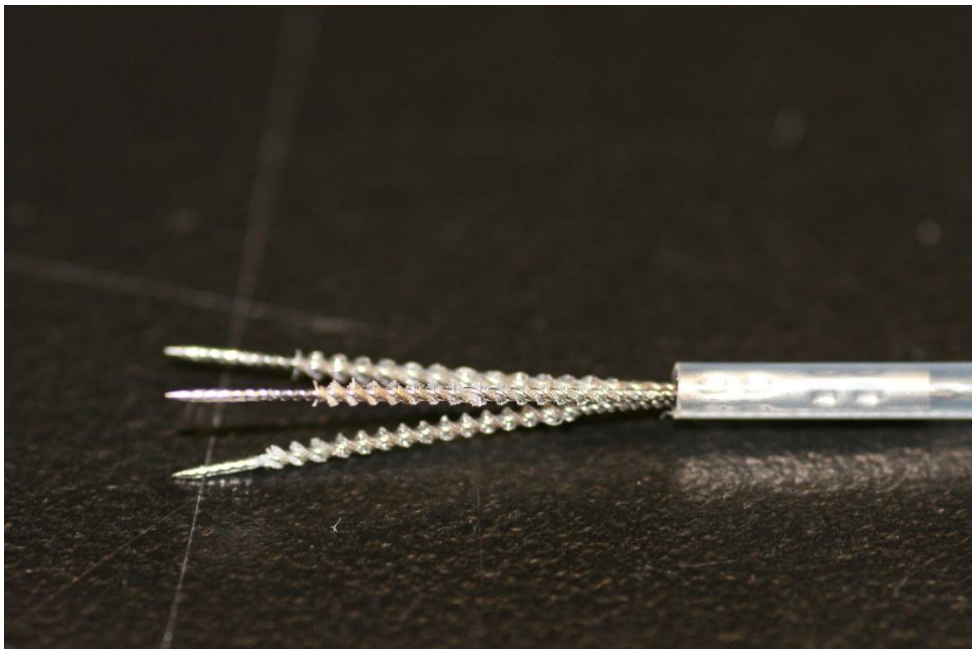

Figure 4: Triple Needle Tipped Brushes in advanced position

The Triple Needle-Tipped Brush is available in two versions.

- Model SDTNB1000 has a 10 mm length from the base of the bristles to the tip of the needle.
- Model SDTNB1500 has a 15 mm length from the base of the bristles to the tip of the needle.

Copies of the design drawings for each of these models are included in Attachment 1.

The product is provided sterile with each device in an individual, labeled, Tyvek pouch as shown in Figure 5. This pouch is Tyvek on one side and a laminated PET (Polyethylene terephthalate) / LDPE (Low Density Polyethylene) film on the other side. The Tyvek pouch has three sides sealed at the pouch manufacturer and one side sealed after the product is placed inside at the contract manufacturer. The pouch is wide enough and long enough to accommodate the finished product in a coiled position. The shelf carton is designed to open on the end to allow access to the contents of the product box. The shelf carton and shipping box protect the product from damage during distribution.

Ten sterile brush packages will be sold together in one shelf carton. This product is intended to be shipped under ambient conditions and does not necessitate any special storage or handling conditions. Copies of the packaging drawings for each model are included in Attachment 2.

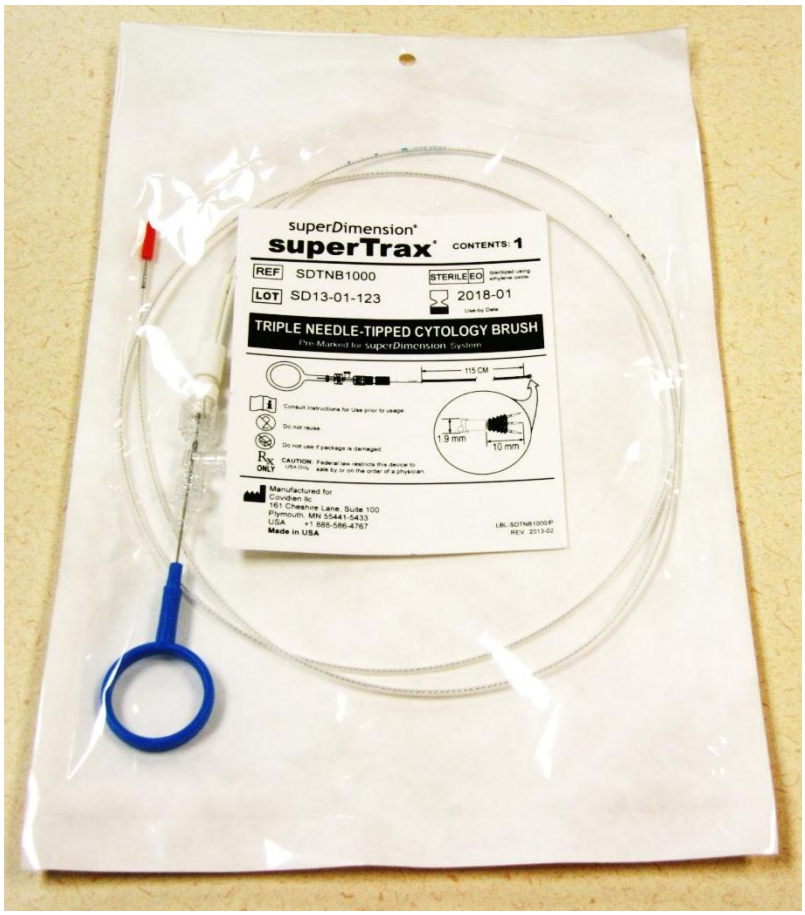

Figure 5: Pouched Triple Needle-Tipped Brush

(b) (4)

[redacted]

Table 2: Component Materials and Determination of Patient Contact

(b) (4)

[redacted]

The design specifications for this product were derived from customer requirements, regulatory requirements, use requirements, and hazard analysis. These specifications are then translated into the design prints and were verified during the development process.

(b) (4) [redacted] Triple Needle-tipped Cytology Brush Tool, Design specification is included in Attachment 3.

Section 9 Substantial Equivalence Discussion

The superTrax® triple needle-tipped brush is substantially equivalent to the Hobbs Bronchial brush and the ConMed Needle-Tip Cytology Brush. A detailed comparison of the features and approvals of these devices are shown in Table 3.

Table 3: Comparison to Predicate Devices

Characteristic	superTrax Triple Needle-Tipped Brush	Hobbs Cytology Brush	ConMed Needle-Tip Cytology Brush
510(k) Clearance	Under review	K834402 Gastrointestinal Sheath Brush	K944650 Wang Bronchial Needle Brush (assumed)[1]
FDA Product Code	BTG Brush Biopsy, Bronchoscope	KOG Endoscope and accessories	EOQ Bronchoscope (Flexible or Rigid) and Accessories
Indication for Use	To be utilized by physician / trained personnel through a flexible endoscope or the superDimension system for retrieving specimens from endobronchial lesions, peripheral lung nodules or lung masses.	To be utilized by a trained physician and / or trained personnel through a flexible endoscope when brush cell samples are required for cytological analysis.	For retrieving cytology specimens from endobronchial lesions, peripheral lung nodules or lung masses using flexible bronchoscopes
Model Number Compared to	SDTNB1000 SDTNB1500	4206	NB-120
Single Use	Single Use	Single Use	Single Use
Contraindications	None	Those associated with Bronchoscopy and GI Endoscopy in gaining access to the desired site Uncooperative Patient	None
Aspiration Port	Yes	No	Yes
Supplied Sterile	Yes	Yes	Yes
Sterilization Technique	Ethylene Oxide	Ethylene Oxide	Ethylene Oxide
Retractable	Yes	Yes	Yes

[1] This 510(k) number is listed as because there is no 510(k) approved for cytology brushes under the ConMed name. ConMed sells other Wang products and is believed to have acquired the rights to market these devices under this 510(k). Literature articles have also linked this product to the Wang device.

Brush			
Retraction Mechanism	Thumb Ring	Thumb Ring	Luer Cap
Outer Sheath Material	ETFE	PTFE	Not Known
Outer Sheath Diameter	1.92 mm	1.70 mm	1.9 mm
Catheter Length	115 cm	120 cm	140 cm
Number of Brushes	Three	One	One
Brush Length	10 mm and 15 mm	13 mm	11 mm
Brush Diameter	.85 mm	3.0 mm	1.7 mm
Sharpened Tips	Yes	No	Yes
Inner Wire Material	304 Stainless Steel	304 Stainless Steel	Not known
Shaft Markers	Present	None	None
Proximal Connector	Luer	Luer	Luer

The superTrax Triple Needle-Tipped brush and both predicate devices are similar in technology and use. The brush configurations differ slightly as shown in Figure 6. In this figure, the top brush is made by Hobbs Medical, the middle brush is the superTrax Triple Needle-Tipped device made for superDimension by Hobbs Medical Inc., and the bottom image is the ConMed Needle-Tipped brush. The superTrax product is basically three miniature ConMed brushes on one core wire. This allows cellular or tissue samples to be taken from a larger area.

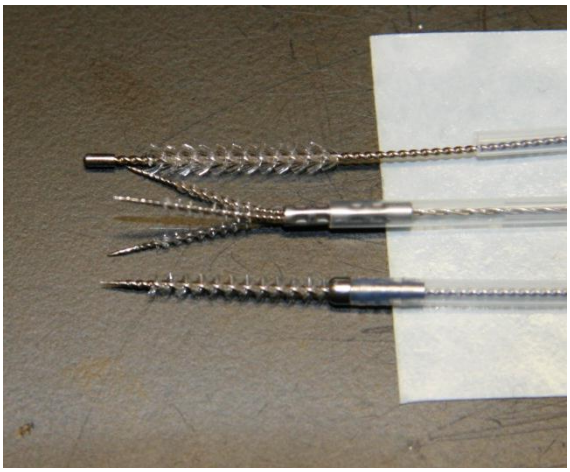

Figure 6: Comparison of Triple Needle-Tipped Brush with Predicate Devices

To insure that the superTrax Triple Needle-tipped brush was similar to the predicate devices, predicate devices were tested to verify the labeled characteristics and to evaluate

performance using the same test methods as used for the superTrax Triple Needle-tipped brush. Dimensional and visual inspections were done along with comparisons of the radiopacity, kinkability, and trackability. Copies of the test protocol, [redacted] esign Verification Test Report, Triple Needle Cytology Brush Predicate Device, are included in Attachment 4.

Additional comparison testing was done to evaluate the predicate and new devices under simulated use conditions. [redacted] In all cases, the cytology brushes were able to collect cell samples. [redacted] he reports detailing this testing, [redacted] Design Validation Test Protocol for Triple Needle- Tipped Cytology Brush and [redacted] Design Validation Test Report for Triple Needle Brush, are included in Attachment 5.

Based on the labeling, physical attributes, and testing data, the superTrax Triple Needle-Tipped Cytology brush is substantially equivalent to the ConMed Needle-Tipped Cytology Brush and the Hobbs Cytology Brush predicate devices in the following attributes:

- Indications for Use
- Design
- Mechanism of action
- Size
- Length
- Materials
- Sterilization technique
- Packaging

The difference between having one and three brushes does not significantly alter the use of the device and could possibly be an improvement over the existing configuration.

Section 10 Proposed Labeling

In accordance with 21 CFR 807.87(e), the labeling for the superTrax Triple Needle-Tipped Brush has been developed to meet the FDA requirements as outlined in the Device Labeling Guidance Blue Book Memo G91-1. Wherever possible, symbols have been used in accordance with ISO 15223-1: 2012 "Symbols to be used with medical device labels, labeling, and information to be supplied" and EN 980:2008 "Symbols for use in the labeling of medical devices." Each pouch is labeled and then ten pouches are placed in a labeled box along with one Instructions for Use (IFU). Copies of the draft pouch and box labels for both models are included Attachment 6 and a copy of the draft IFU used for both models is included in Attachment 7.

Section 11 Sterilization and Shelf Life

Sterilization Method:

Hobbs Medical is the contract manufacturer for the superDimension superTrax Triple Needle-Tipped Cytology Brush. They currently manufacture one of the predicate devices, the Hobbs Cytology Brush (K834402). The sterilization of this product is being adopted into the same validated ethylene oxide sterilization cycle as the Hobbs Cytology Brush due to the equivalency with existing products. The Hobbs Medical Cytology Brushes are currently sterilized at Steris Isomedix in S. Plainfield, New Jersey. The superTrax Triple Needle-Tipped Cytology brush will be manufactured and sterilized at the same facility using the same process. Based on AAMI TIR 28:2009 Annex A, a complete analysis of the candidate product was completed prior to adoption into the sterilization cycle. This analysis was completed by Hobbs Medical, Inc. for the superTrax Triple Needle-Tipped Cytology Brush. They concluded that the sterilization process could be adopted since:

- The materials are identical to the current Hobbs product.
- Triple Needle-Tipped Brush is less of a challenge than other currently sterilized product such as the Microbiology Brush.
- Packaging is identical to current product.

As part of the annual sterilization revalidation, additional testing specific to the superTrax Triple Needle-tipped brush was done to validate acceptability of the process and collect baseline data on ethylene oxide residuals and bioburden levels.

Sterility Assurance Level:

The validation was designed to ensure that the Triple Needle Brush exceeds a sterility assurance level (SAL) of 10^{-6}.

Sterilization Validation:

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[redacted]

(b) (4)

[redacted]

When the half-cycle successfully sterilizes all of the products and the 10^6 B. *atrophaeus* biological challenges then, the full cycle will provide a significant overkill and margin of safety. The bioburden testing was done in accordance with ISO 11737-1 and the sample size for the BI spore strips was in accordance with ISO 11135-1 for the chamber being used. The success criteria for the revalidation were:

- The half-cycle and full-cycle must achieve time, temperature and humidity parameters, and gas concentration as specified in the respective current Steris cycle parameters.
- No growth must be detected in the twenty inoculated SDTNB1500 brushes, the 18 biological indicators, or the 26 USP sterility samples from the full cycle.
- Mean bioburden levels must be less than 1000 CFU/device.
- Post-quarantine (Day 7 post-sterilization) Ethylene oxide residual levels must meet ISO 10993-7 requirements for short-term use, mucosal contact products.

Sterility Testing Results:

After the half cycle, the sterilization showed no growth detected from the 18 EPCD (External Process Challenge devices), 20 IPCD (Internal Process Challenge Device - superDimension Triple Needle Tipped brush), or 30 half cycle product samples. All controls tested as expected.

During the full cycle testing, no growth was detected in the eighteen biological indicators thus demonstrating that the sterility assurance level for this product is acceptable and can be adopted into the existing Hobbs Medical sterilization cycle.

Bioburden Results:

Three lots of ten products each were tested for bioburden. All results were substantially below the acceptance level of 1000 CFU/device. The results are shown in the table below.

Table 4: Bioburden Results

Lot	Aerobic Bacteria Mean CFU / Device	Yeast and Mold Mean CFU / Device	Total Mean Bioburden (Aerobic Count + Yeast & Molds) CFU
Acceptance Criteria	N/A	N/A	Mean <1,000 CFU
#1	(b) (4)		

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Ethylene Oxide Residuals:

Ethylene Oxide Residuals were tested in accordance with ISO 10993-7:2008. Ethylene oxide (EtO) residual and Ethylene Chlorohydrin (ECH) were tested at the end of the seven day quarantine. Three samples were tested after the first sterilization cycle and three samples after the second sterilization cycle. The samples were pooled together for testing with the results as follows:

Table 5: Ethylene Oxide Residual Results

Sample Lot Number	Ethylene Oxide mg/sample	Ethylene Chlorohydrin mg/sample
Acceptance Criteria	4 mg. (from ISO 10993-7 Annex	9 mg. (from ISO 10993-7 Annex

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Endotoxin Testing:

Endotoxin testing was not done on the superTrax Triple Needle Cytology brush as it does not contact circulating blood or cerebrospinal fluid, and is not an intraocular product or used in *in vitro* fertilization. No claims to be "pyrogen free" are being made.

Packaging Description:

The superTrax Triple Needle-Tipped Cytology Brush is contract manufactured at Hobbs Medical for superDimension using the same Tyvek pouch as currently used on other cytology brush products that they produce. This pouch is Tyvek on one side and a laminated PET (Polyethylene terephthalate) / LDPE (Low Density Polyethylene) film on the other side. The Tyvek pouch has three sides sealed at the pouch manufacturer and

one side sealed at the product manufacturer. The pouch is wide enough and long enough to accommodate the finished product in a coiled position. The shelf carton is designed to open on the end to allow access to the contents of the product box. The shelf carton and shipping box protect the product from damage during distribution. This product will be a single use product and resterilization or reuse is not allowed.

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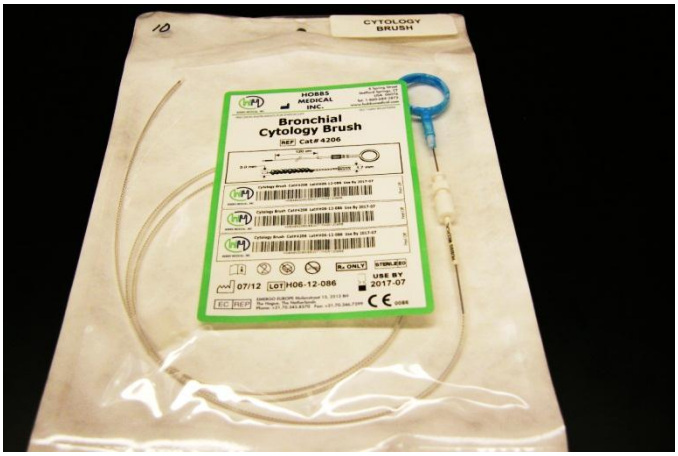

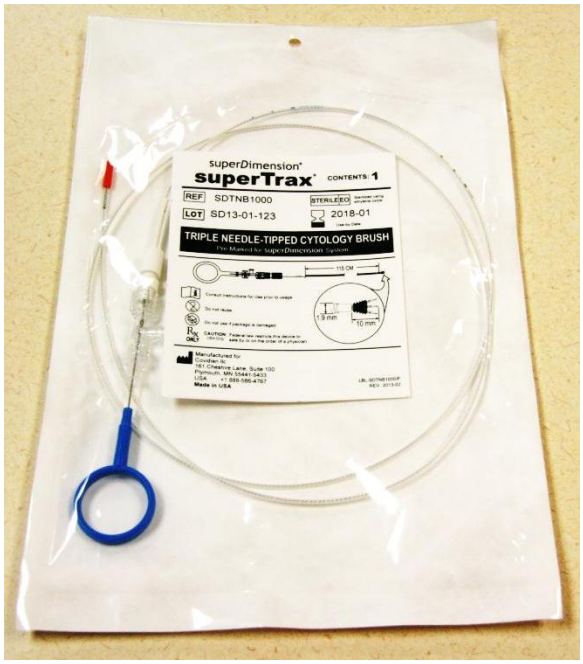

Figure 8: superTrax Triple Needle- Tipped Cytology Brush Package

Figure 9: superTrax Triple Needle-Tipped Cytology brush box

(b) (4) Testing

(b) (4) Testing

Section 12 Biocompatibility

Based on ISO 10993-1:2009 the Triple Needle-Tipped Cytology Brush will be classified using on the following criteria:

(b) (4)

Given the category, contact, and contact duration, only three biocompatibility tests are deemed necessary as shown in the table below. All others are not required testing based on the standard and in consideration of the history and low risk of this device. Per ISO 10993-1, an evaluation of all biocompatibility tests was completed and the assessment of relevancy is shown in the following table.

(b) (4)

(b) (4)

An evaluation of the product materials and usage was completed in conjunction with NAMSA to determine the best possible way to test the Triple Needle-Tipped Brush. The Triple-Needle Brush is inserted into an Extended Working Channel (EWC) or flexible bronchoscope which acts as a conduit to the sampling site. Once the Triple Needle-Tipped Brush is at the desired location, the brush is then extended out of the sheath to collect a cell sample then retracted back within the sheath. Once the sample is collected the entire brush is removed from the EWC.

The duration that the Triple Needle-Tipped Brush is within the body is probably less than ten minutes and more likely only a few minutes. The inside of the cytology brush is not likely to have any contact with the patient as the crimp blocks off the tube entrance. In some cases, a tiny amount of air could possibly get into this space if the pulmonologist uses the aspiration port.

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(b) (4)

(b) (4)

[redacted]

Acceptance criteria for each test were according to the relevant standard. Because each test is based on a spectrum without absolute pass / fail criteria, final acceptance was based on scientific judgment, comparison with control samples, and standard practices.

The conclusions drawn from the biocompatibility testing were as follows:

Table 8: Biocompatibility Test Results

Test	Test Conclusion
ISO Guinea Pig Maximization Sensitization Test	The test article extracts showed no evidence of causing delayed dermal contact sensitization in the guinea pig. The test article was not considered a sensitizer in the guinea pig test.
Cytotoxicity Study Using the ISO Elution Method	The test article extract showed no evidence of causing cell lysis or toxicity. The test article extract met the requirements of the test since the grade was less than a grade 2 (mild reactivity)
ISO Vaginal Irritation Study in Rabbits	The sodium chloride and sesame oil test article extracts were considered a nonirritant to vaginal tissue of the rabbit.

A copy of the biocompatibility test report is included in Attachment 9 and includes the original biocompatibility reports from NAMSA.

Section 13 Software

There is no software associated with this product so this section is not applicable.

Section 14 Electromagnetic Compatibility and Electrical Safety

This device does not include an electronic component so this section is not applicable.

Section 15 Performance Testing – Bench

In order to demonstrate safety and performance of the superTrax Triple Needle-Tipped Brush, substantial design verification testing was completed. A summary of these test methods and results are detailed in the following table with the complete protocols and (b) (4) included in Attachment 10.

Table 9: Performance Testing Bench Results

(b) (4)

(b) (4)

[redacted]

[1] One brush had a few loose bristles that caused the length requirement to not be met for that device. Loose bristles were addressed in the supplemental testing protocol through process validation.

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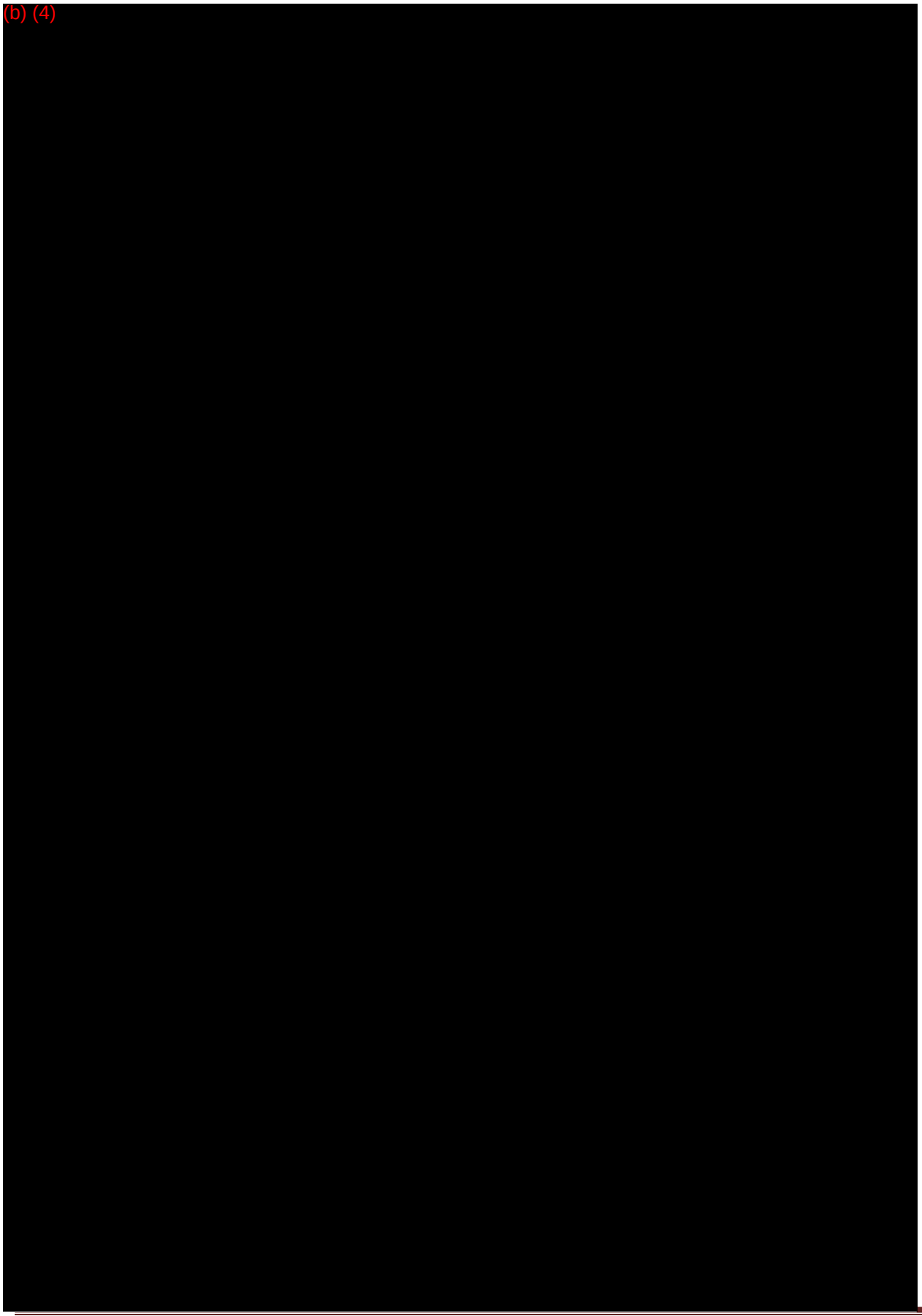

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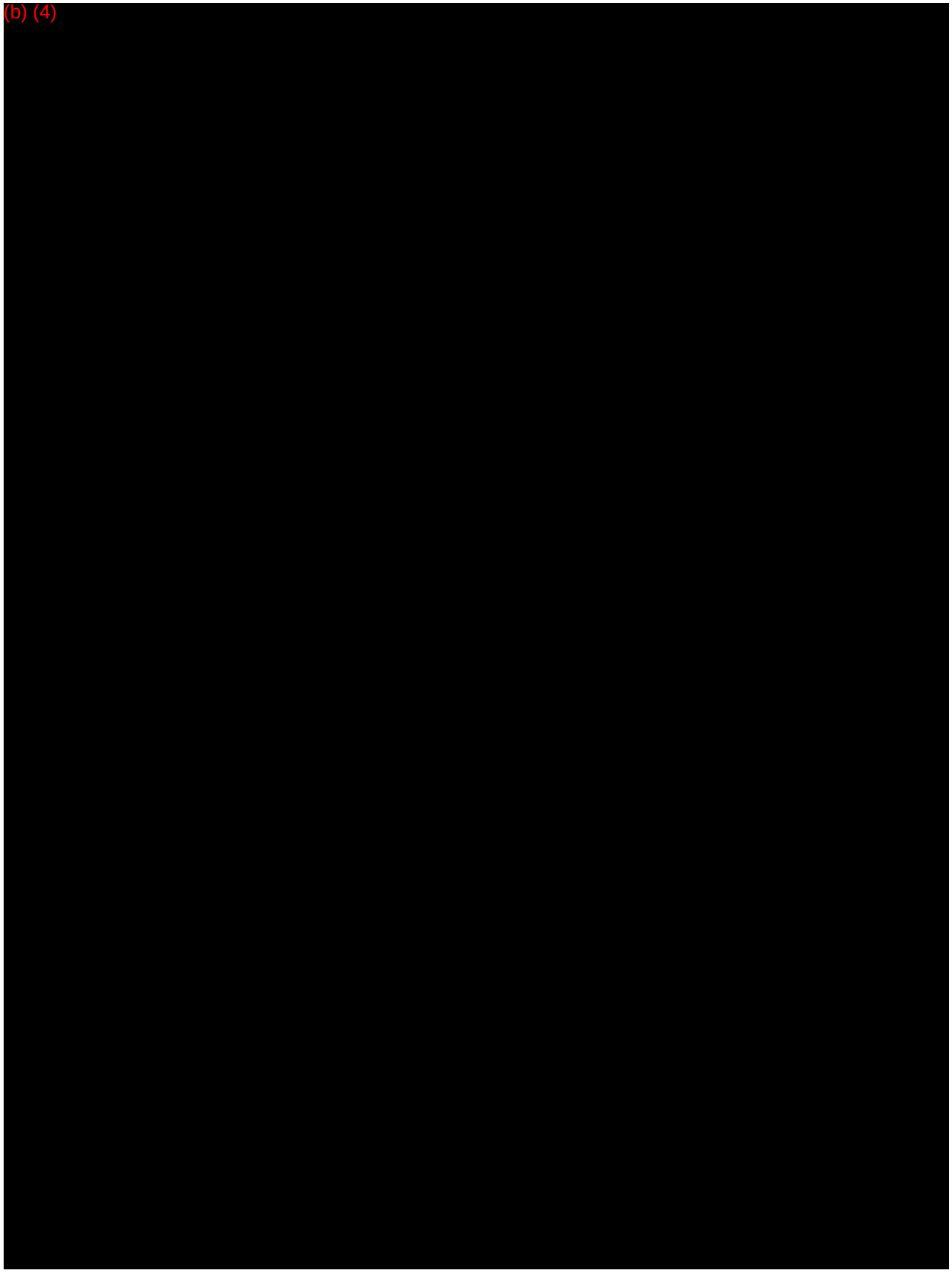
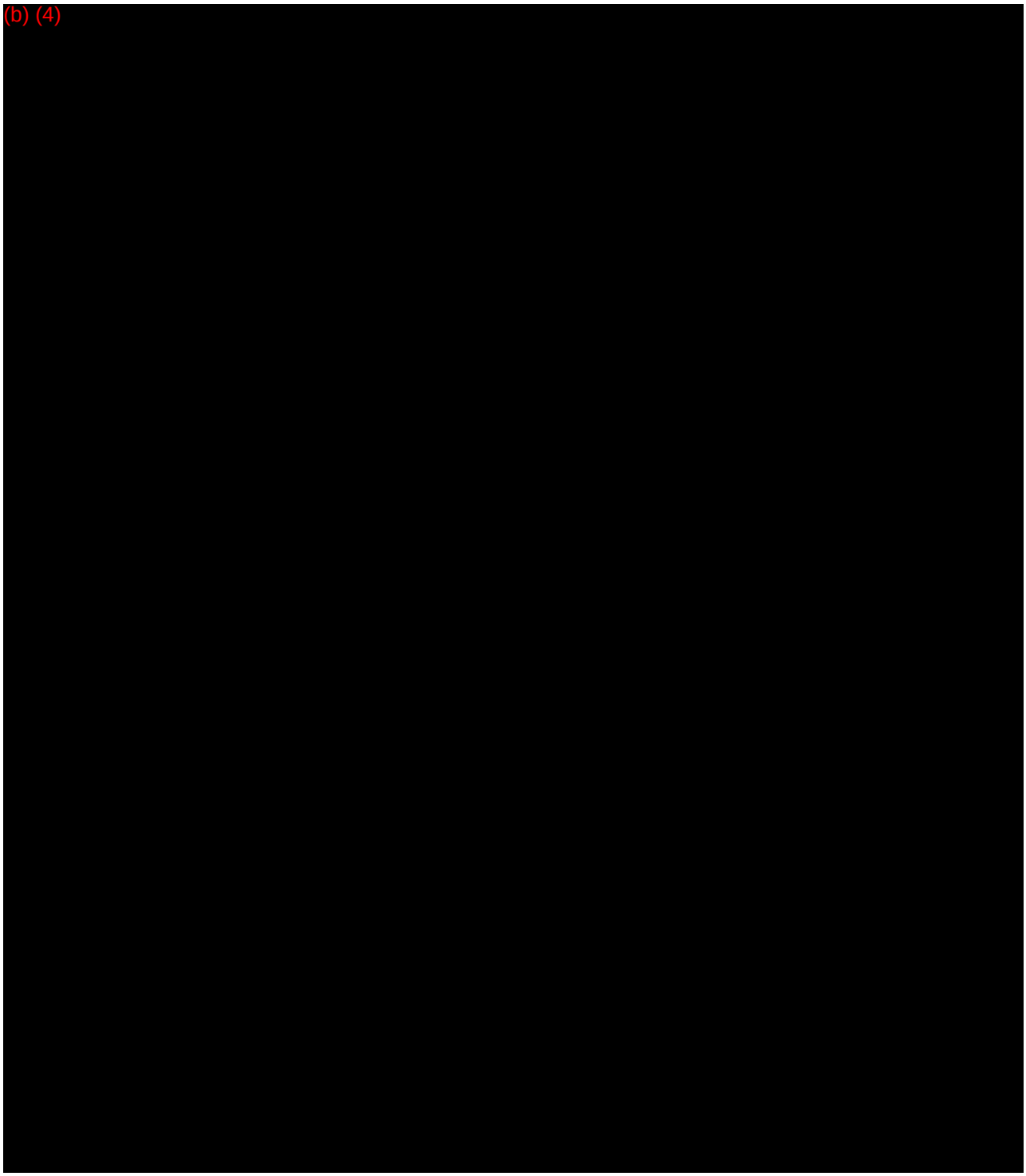
(b) (4)



(b) (4)



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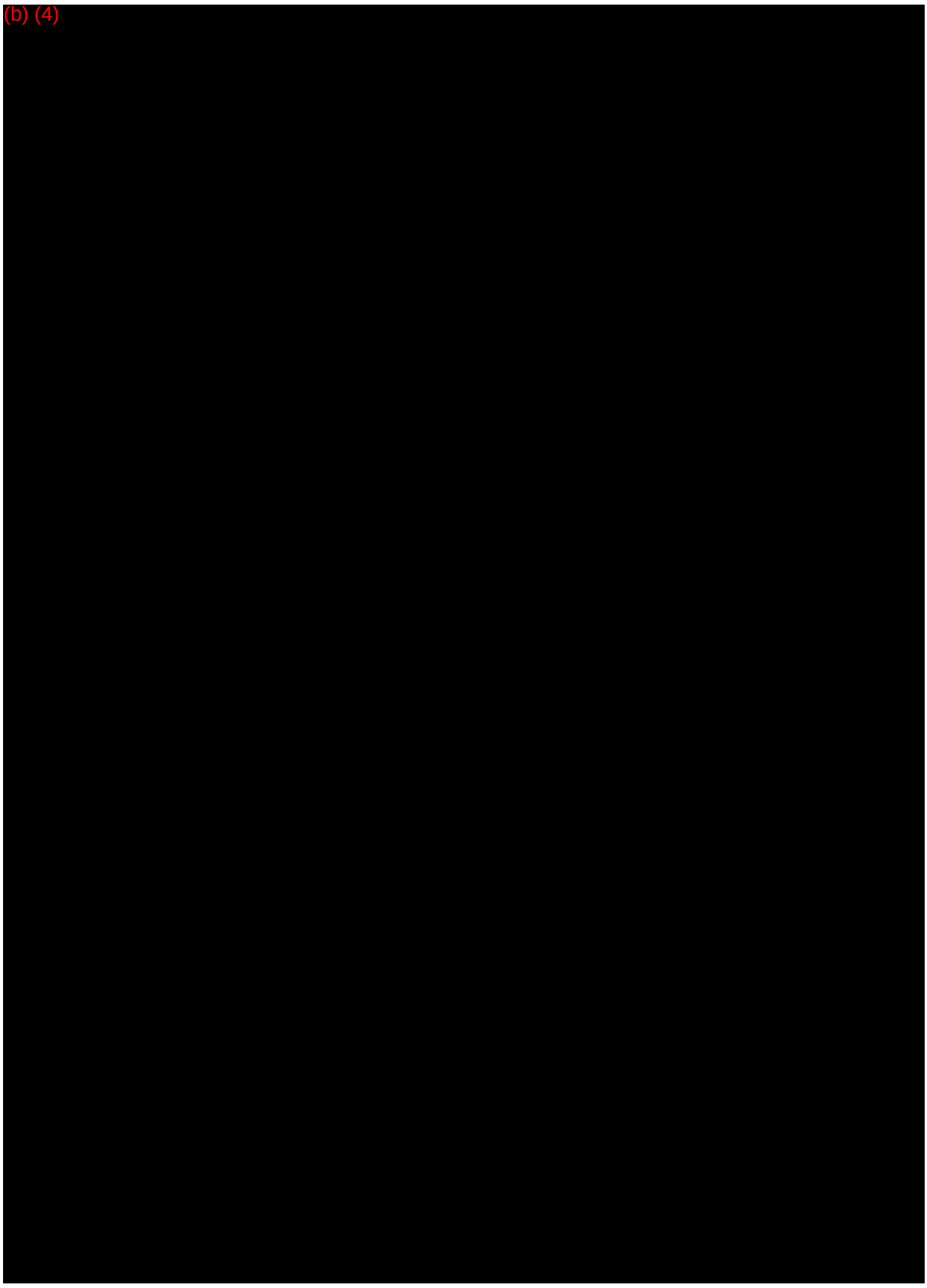

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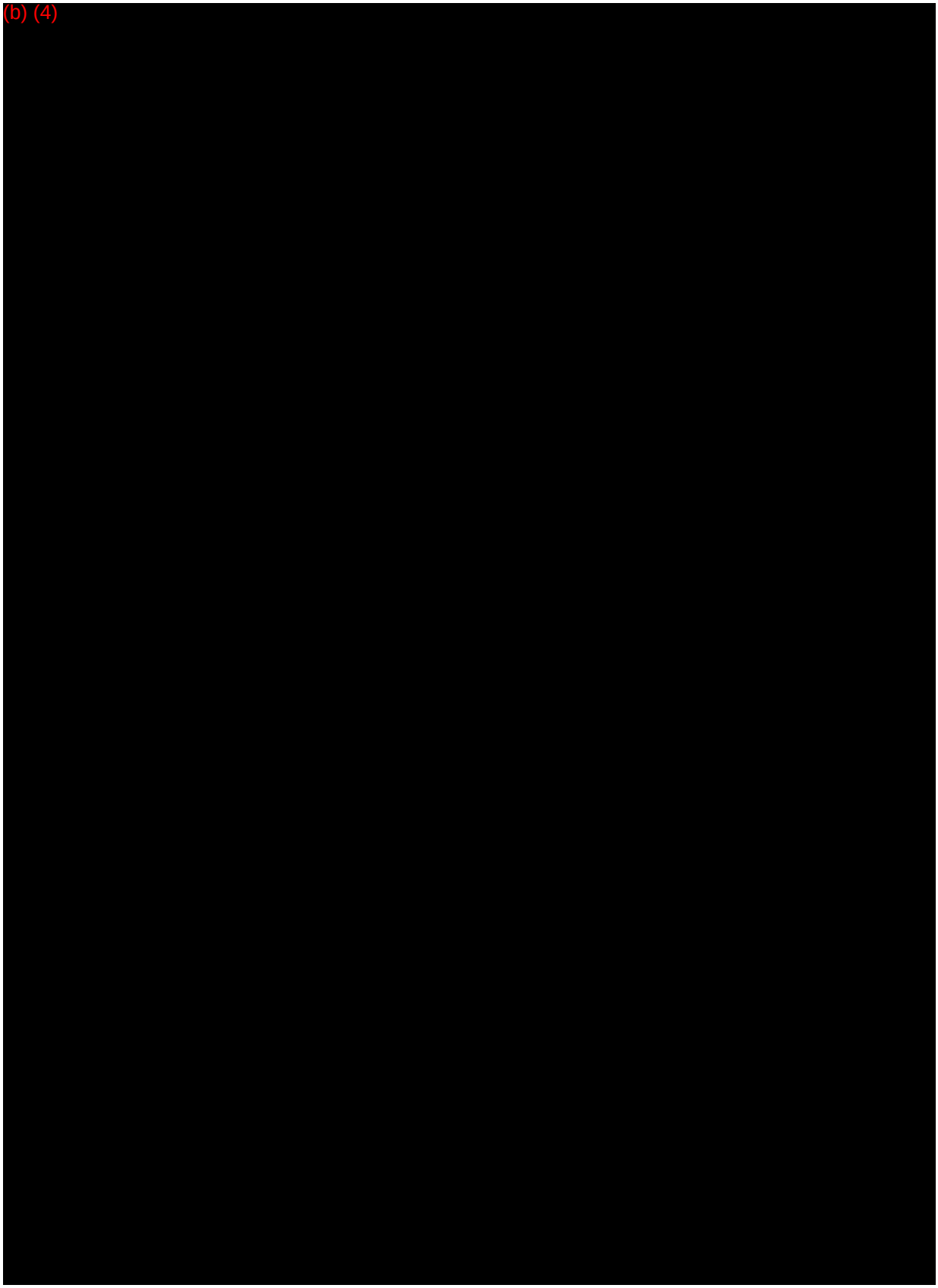

(b) (4)

The superTrax Triple Needle-Tipped Cytology Brush successfully passed all of the bench top performance tests by meeting the required acceptance criteria. All aspects of the design have been tested to verify safety and bench top performance in accordance with the superDimension quality system requirements.

Section 16 Performance Testing – Animal

No performance testing was done on animals as part of the pre-clinical testing so this section is not applicable.

Section 17 Performance Testing - Clinical

There was no clinical testing done on this product so this section is not applicable.

Attachment 1

Design Drawings

Contents:

(b) (4)

(b) (4)

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(b) (4)

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Attachment 2

Package Drawings

Contents:

(b) (4)

(b) (4)

Attachment 3

Design Specification

Contents:

Triple Needle-tipped Cytology Brush Biopsy Tool Design Specification

Table of Contents

		Revisio	(b) (4)
Document Title:	Triple Needle-tipped Cytology Brush Biopsy Tool, Design Specification	Effectiv	
Owner:			
Author:	(b) (4), (b) (6)		

1 Introduction

1.1 Purpose

This document identifies the requirements for the triple needle tipped cytology brush biopsy tool.

1.2 Scope

This document covers the device requirements, and the specifications, of the triple needle tipped cytology brush. The triple needle tipped cytology brush consists of two components: the inner catheter assembly and the outer catheter assembly. The inner catheter assembly will have a thumb ring at the proximal end and a twisted wire shaft to connect to the distal end that will contain 3 individual needle tipped cytology brushes. The outer catheter assembly will be a sheath to cover the sharp distal section of the inner catheter, will be pre-marked for EWC lengths and will terminate at the proximal end at a luer fitting that can be used for aspiration.

(b) (4)

The product requirements document business section, SDTNB-B1 through SDTNB-B6, is primarily project goals and not formal product requirements and will not be formally addressed as design specifications. They will also not be a part of design verification or validation. Some of the project goals are repeated in subsequent sections later in the product requirements and those will be addressed as design specifications and will be addressed in formal design verification and/or validation.

1.3 Definitions, Acronyms, Abbreviations

PR	Product Requirements
DI	Design Input
ENB	Electromagnetic Navigation Bronchoscopy
EWC	Extended Working Chanel
LG	The Locatable Guide – sensor catheter
ID	Identification
N/A	No applicable requirements in the specific section
P/N	Part Number
sD	superDimension
SU	Single Use
Target	Designated area in the lung (which the physician select during planning)
TNB	Triple Needle Brush
HMI	Hobbs Medical Inc.

1.4 Design Input References

The following documents form a part of this specification to the extent specified herein. In the event of conflict between the documents referenced herein and the contents of this specification, the contents of this specification shall be considered a superseding requirement.

(b) (4)

2 Design Specifications

2.1 Overview

The triple needle tipped cytology brush consists of two components: the inner catheter assembly and the outer catheter assembly. The inner catheter assembly will have a thumb ring at the proximal end and a twisted wire shaft to connect to the distal end that will contain 3 individual needle tipped cytology brushes. The outer catheter assembly will be a sheath to cover the sharp distal section of the inner catheter, will be pre-marked for EWC lengths, and will terminate at the proximal end at a luer fitting that can be used for aspiration.

The triple needle-tipped cytology brush will be manufactured by Hobbs Medical, placed into one device per package and sealed in a single barrier pouch, and delivered as a finished sterile product in boxes of 10 devices each, very similar to existing brush products currently private label from Hobbs Medical.

2.1.1 Operational Use

The triple needle-tipped cytology brush will be placed within the body to sample tissue from a target location more broadly than a traditional single cytology brush. The triple needle tipped cytology brush could be used by itself or in conjunction with the superDimension ENB system.

Use with the superDimension ENB system: After successfully navigating to the targeted site in the lungs, the LG would be removed. The triple needle tipped cytology brush biopsy procedure would consist of three steps:

Advancing the catheter out of the EWC close to the target site

Extending the inner catheter with the triple brushes out of the outer sheath to drive the cytology brush into the target location

Retracting the inner catheter into the outer sheath and withdrawing the entire device from the EWC

Use without the superDimension ENB system: after successfully identifying the target the above procedure would be repeated using the instrument channel of a flexible bronchoscope or endoscope.

2.1.2 Approvals and Regulatory Classifications

FDA – Class II 510(k)
EUROPE – Class IIa per rule 7 per 93/42/EEC Medical Device Directive Annex IX

2.1.3 Product Compatibility Requirements

(b) (4)

2.2 Design Performance and Configuration Specifications

(b) (4)

(b)(4) Specifications

(b)(4) Specifications

(b)(4) Specifications

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(b)(4) Specifications

Attachment 4

Predicate Device Testing

Contents:

(b) (4) Design Verification, Triple Needle Cytology Brush Predicate Devices Test Protocol

(b) (4) Design Verification Test Report, Triple Needle Cytology Brush Predicate Devices Test Protocol

		Revision (b) (4)
Document Title:	Design Verification Test Report, Triple Needle Cytology Brush Predicate Device	Effective
Owner:	Research & Development	Page 1 of 21
Author:	(b) (4), (b) (6)	

Design Verification Test Report, Triple Needle Cytology Brush Predicate Device

Table of Contents

1.0 PURPOSE

The purpose of this document is to deta predicate device testing done according (b) (4) [redacted]

2.0 DEFINITIONS / ACRONYMS / ABBREVIATIONS

2.1 P/N: Part Number
2.2 L/N: Lot Number
2.3 OD: Outer Diameter
2.4 ID: Inner Diameter
2.5 OAL: Overall Length
2.6 TNB: Triple Needle Brush
2.7 Assy: Assembly
2.8 HMI: Hobbs Medical, Inc.
2.9 N/A: Not Applicable
2.10 EWC: Extended Working Channel
2.11 NB: Needle Brush

(b) (4) [redacted]

	[redacted]	Revision	(b) (4) [redacted]
Document Title:	Design Verification Test Report, Triple Needle Cytology Brush Predicate Device	Effective	
Owner:			
Author:	(b) (4) [redacted]		

4.0 SUMMARY OF TESTING ACTIVITIES

(b) (4) [redacted]

5.0 TEST ENVIRONMENT

(b) (4) [redacted]

6.0 TEST EQUIPMENT / MATERIALS / TOOLS

(b) (4)

(b) (4) Testing

(b) (4) Testing

(b) (4) Testing

(b) (4) Testing

(b) (4) Testing

(b) (4) Testing

(b) (4) Testing

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(b) (4) Testing

(b) (4) Testing

(b) (4) Testing

(b) (4) Testing

(b) (4) Testing

11.0 CONCLUSIONS

The outer sheaths and the brushes of the devices were measured and the dimensional values documented.

Neither predicate device had any markings on the outer sheath.

Each device had one brush.

The tip of the Hobbs Medical Cytology Brush Model #4206 was blunt.

The tip of the ConMed Cytology Brush Model NB-120 was sharpened.

Both predicate devices were visible under Fluoroscopy.

The ConMed Cytology Brush Model NB-120 was trackable to all sites without resultant kinking.

The Hobbs Medical Cytology Brush Model #4206 was trackable to all sites without resultant kinking.

This evaluation was designed to detail test results rather than making a decision of pass/fail, therefore, there was no acceptance criteria.

(b) (4) Testing

(b) (4) Testing

(b) (4) Testing

Attachment 5

Design Validation Testing

Contents:

(b) (4)

Design Validation Test Protocol for Triple Needle Tipped Cytology Brush
Design Validation Test Report for Triple Needle Brush

	[redacted]	Revision (b) (4)
Document Title:	Design Validation Test Protocol for Triple Needle Tipped Cytology Brush	Effective [redacted]
Owner:	Research and Development	Page 1 of 10
Author:	(b) (4), (b) (6) [redacted]	

Design Validation Test Protocol for Triple Needle Tipped Cytology Brush

Table of Contents

		Revision	(b) (4)
Document Title:	Design Validation Test Protocol for Triple Needle Tipped Cytology Brush	Effective	
Owner:			
Author:	(b) (4), (b) (6)		

1.0 PURPOSE

This document is the design validation test for the triple needle tipped cytology brush. The document describes the test environment, test equipment, and test protocols to be used in order to perform the design validation for the triple needle tipped cytology brush.

2.0 DEFINITIONS / ACRONYMS / ABBREVIATIONS

EWC	Extended Working Channel
sD	superDimension
N/A	Not Applicable
TNB	Triple Needle Brush
SLM	Simplified Lung Model

3.0 REFERENCES

(b) (4)

4.0 SUMMARY OF TESTING ACTIVITIES

(b) (4)

5.0 TEST ENVIRONMENT

The test is performed within superDimension premises. This test environment will simulate a standard operating, endoscopy, and bronchoscopy room.

6.0 TEST EQUIPMENT / MATERIALS / TOOLS

(b) (4) [redacted]

7.0 TEST ARTICLES

The test articles and test equipment are detailed above (See section 6.0 above).

8.0 SAMPLE SIZE DETERMINATION

8.1 (b) (4) [redacted]

(b) (4) Protocols, (b) (4) Testing

(b) (4) Protocols, (b) (4) Testing

(b) (4) Protocols, (b) (4) Testing

(b) (4) Protocols, (b) (4) Testing

10.0 ACCEPTANCE CRITERIA

10.1 The simulated biopsy test is considered successful (Pass) if the test articles are placed successfully through the channel (Edge EWC and bronchoscope) into the simulated lung tissue and there is visible evidenc (b) (4) [redacted] cytology brushes. The test articles under test are just the triple needle brush models. The two other test articles (cytology brushes) are the predicate devices for regulatory purposes, these cytology brushes will not have acceptance criteria but the cell retention on the brushes may be compared to the triple cytology brushes.

11.0 TEST PROTOCOL TRACEABILITY

N/A

12.0 TEST FORMS

Simulated Biopsies with test articles performed and cells were visible (EC = Edge Catheter BS = Bronchoscope)										
Cytology Brush Model	EC 1	EC 2	EC 3	EC 4	EC 5	BS 1	BS 2	BS 3	BS 4	BS 5
SDTNB1000	Y / N	Y / N	Y / N	Y / N	Y / N	Y / N	Y / N	Y / N	Y / N	Y / N
SDTNB1500	Y / N	Y / N	Y / N	Y / N	Y / N	Y / N	Y / N	Y / N	Y / N	Y / N
4206 – Hobbs Medical	Y / N	Y / N	Y / N	Y / N	Y / N	Y / N	Y / N	Y / N	Y / N	Y / N
NB-120 ConMed	Y / N	Y / N	Y / N	Y / N	Y / N	Y / N	Y / N	Y / N	Y / N	Y / N

Printed Name: _____

Signature: _____

Date Completed: _____

12.1 TEST ARTICLE/EQUIPMENT FORM

(b) (4)

[redacted]

Initials /Date _____

	[redacted]	Revision
Document Title:	Design Validation Test Report Triple Needle Brush	Effectiv
Owner:	Research and Development	Page 1 o
Author:	(b) (4), (b) (6)	

Design Validation Test Report for Triple Needle Brush

Table of Contents

1.0 PURPOSE

The purpose of this report is to present test results against the referenced protocol, when using the Triple Needle Brush products manufactured by Hobbs Medical. Additionally, two predicate devices were tested for comparison.

2.0 REFERENCES

[A1] (b) (4)

3.0 TEST DATA

(b) (4)

(b) (4)

4.0 ANALYSIS OF RESULTS

The acceptance criteria for the Triple Needle Brush were defined in the protocol as requiring the test articles to successfully pass through th
containing visible evidence (b) (4) on the cytology brushes upon withdrawal. The test articles under test are just the triple needle brush models. There were no criteria for the competitive, predicate devices which were included for comparative purposes only. All acceptance criteria specified in the protocol have been met.

5.0 PROTOCOL DISCREPANCIES

(b) (4)

6.0 CONCLUSION

The Triple Needle Brush product collected tissue from the simulated lung material while being used through the Edge catheter and the bronchoscope when tested per the above referenced protocol. There was no attempt to quantify the amount of tissue due to the complexity of these techniques. The predicate devices tested as part of the above protocol were for comparative purposes and did not have any formal acceptance criteria.

The table below shows how the customer requirements were fulfilled by this testing.

(b) (4)

7.0 **APPENDIX A --**Manufacturing documents

(b) (4)

Attachment 6

Pouch and Box Labels

Contents:

Label_SuperTrax-SDTNB1000_Pouch

superDimension®

superTrax®

CONTENTS: 1

REF SDTNB1000

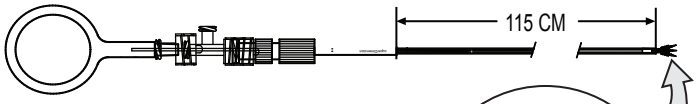
STERILE EO Sterilized using ethylene oxide.

LOT XX##-##-###

YYYY-MM
Use-by Date

TRIPLE NEEDLE-TIPPED CYTOLOGY BRUSH

Pre-Marked for superDimension® System

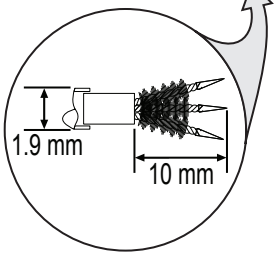


Consult Instructions for Use prior to usage.

Do not reuse.

Do not use if package is damaged.

℞ ONLY **CAUTION:** Federal law restricts this device to sale by or on the order of a physician.
USA Only



Manufactured for
Covidien llc
161 Cheshire Lane, Suite 100
Plymouth, MN 55441-5433
USA +1 888-586-4767
Made in USA

LBL-SDTNB1000/P
REV. 2013-02

Label_SuperTrax-SDTNB1500_Pouch

superDimension®

superTrax®

CONTENTS: 1

REF SDTNB1500

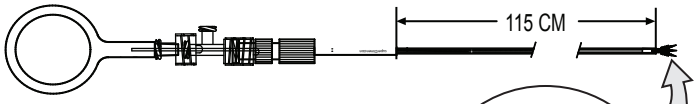
STERILE EO Sterilized using ethylene oxide.

LOT XX##-##-###

YYYY-MM
Use-by Date

TRIPLE NEEDLE-TIPPED CYTOLOGY BRUSH

Pre-Marked for superDimension® System

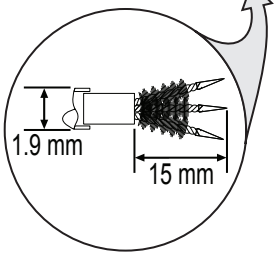


Consult Instructions for Use prior to usage.

Do not reuse.

Do not use if package is damaged.

℞ ONLY **CAUTION:** Federal law restricts this device to sale by or on the order of a physician.
USA Only



Manufactured for
Covidien llc
161 Cheshire Lane, Suite 100
Plymouth, MN 55441-5433
USA +1 888-586-4767
Made in USA

LBL-SDTNB1500/P
REV. 2013-02

Label_SuperTrax-SDTNB1000_Box

superDimension®

superTrax®

CONTENTS: 10

REF SDTNB1000

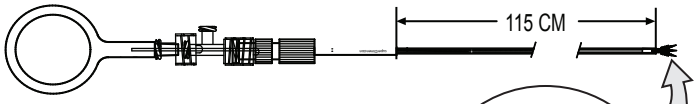
STERILE EO Sterilized using ethylene oxide.

LOT XX##-##-###

YYYY-MM
Use-by Date

TRIPLE NEEDLE-TIPPED CYTOLOGY BRUSH

Pre-Marked for superDimension® System

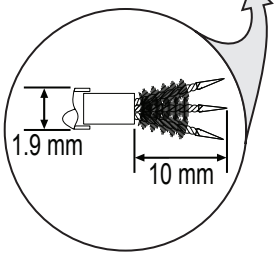


Consult Instructions for Use prior to usage.

Do not reuse.

Do not use if package is damaged.

℞ ONLY **CAUTION:** Federal law restricts this device to sale by or on the order of a physician.
USA Only



Manufactured for
Covidien llc
161 Cheshire Lane, Suite 100
Plymouth, MN 55441-5433
USA +1 888-586-4767
Made in USA

LBL-SDTNB1000/B
REV. 2013-02

Label_SuperTrax-SDTNB1500_Box

superDimension®

superTrax®

CONTENTS: 10

REF SDTNB1500

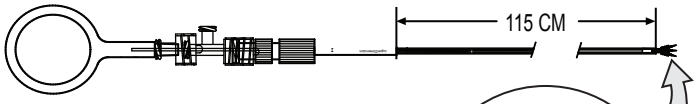
STERILE EO Sterilized using ethylene oxide.

LOT XX##-##-###

YYYY-MM
Use-by Date

TRIPLE NEEDLE-TIPPED CYTOLOGY BRUSH

Pre-Marked for superDimension® System

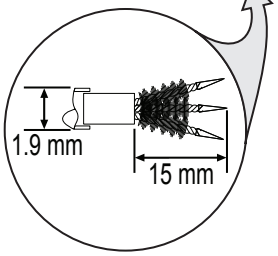


Consult Instructions for Use prior to usage.

Do not reuse.

Do not use if package is damaged.

℞ ONLY **CAUTION:** Federal law restricts this device to sale by or on the order of a physician.
USA Only



Manufactured for
Covidien llc
161 Cheshire Lane, Suite 100
Plymouth, MN 55441-5433
USA +1 888-586-4767
Made in USA

LBL-SDTNB1500/B
REV. 2013-02

Attachment 7

Instructions for Use

Contents:

superDimension®

superTrax®

TRIPLE NEEDLE-TIPPED CYTOLOGY BRUSH

SDTNB1000
SDTNB1500

INSTRUCTIONS FOR USE

Manufactured for
Covidien llc
161 Cheshire Lane, Suite 100
Plymouth, MN 55441-5433
USA
Office: +1 800-387-9016
Fax: +1 866-706-9639
Email: info.us@superdimension.com
Web: www.superdimension.com

Made in USA

COM-1178 Revision A
2013-02

READ CAREFULLY BEFORE USING

Symbols

Symbols are used to highlight safety points and other important information. The symbols may be found on packaging, labeling, or the instrument. The following symbols are used:


Consult instructions for use.


WARNING: Indicates a potentially hazardous situation that – if not avoided – could result in death or serious injury.


CAUTION: Indicates a potentially hazardous situation that could result in injury or damage to the device or equipment.

Sterilized using ethylene oxide.


Do not re-use.


Do not use if package is damaged.


Use-by date.

Batch code.

Catalogue number.

CAUTION: Federal (USA) law restricts this device to sale by or on the order of a physician.

Device Description

The triple needle-brush is designed to provide the ideal combination of high specimen yield and ease of use. This device features Ethylene Tetrafluoroethylene (ETFE) sheathing and sharpened tips that can be used to penetrate tissue to obtain tissue or cell samples.

Safety

Indications for Use

To be utilized by a physician / trained personnel through a flexible endoscope or the superDimension system for retrieving specimens from endobronchial lesions, peripheral lung nodules, or lung masses.

Contraindications

None known.

superDimension®

Precautions

CAUTION: Excess pressure or force applied may cause damage to either the device or the biopsy channel.

CAUTION: Use of this device is restricted to devices or equipment with a biopsy channel minimum inside diameter of 2.08 mm (0.082 inch).

Instructions for Use

1. Open the pouch and remove the small tip protector from the cannula's distal end. **Save the product batch code (lot number) for future reference.**
2. Inspect for any functional abnormality. If any irregularities are noted, call Covidien for a return authorization number.
3. Gently slide the proximal end to ensure the device extends and retracts smoothly.

NOTE: *Twisting or turning the thumb ring handle is not necessary for this device.*

4. Observe and note the position stops for the extended and retracted positions.
5. If aspiration is desired, securely attach a luer-lock syringe to the luer-lock fitting on the proximal end. To aspirate:

5 (a). Insert the device's distal tip, in the retracted position, into the extended working channel (EWC) or other biopsy channel.

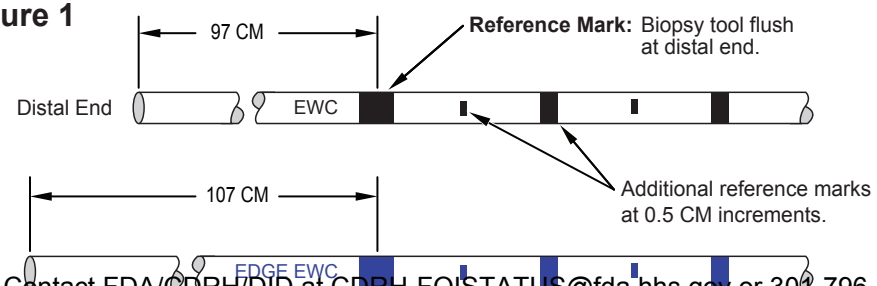
5 (b). Use short, 2 cm strokes to advance the device until reaching the appropriate reference mark on the catheter body.

NOTE: *Refer to Figure 1 for examples of the superDimension EWC black reference marks or Edge™ catheter blue reference marks.*

6. To obtain a specimen, use the thumb ring to extend the device. There is a 2 cm range of motion while moving the handle.
7. When the specimen is obtained, retract the device into the cannula. Remove the device from the biopsy channel keeping the device in the retracted position.
8. Hold the device's distal tip over prepared slides before retrieving the specimen.
9. Follow your health care facility sharps protocol and discard the contaminated device.

CAUTION: Covidien's single-use devices are designed and warranted for one-time use. To avaoid potential infection or cross-contamination, do not reuse this device. Any device re-use is the end user's responsibility.

Figure 1



Attachment 8

Packaging Verification Testing

Contents:

(b) (4)

ackage Testing Protocol for Hobbs Medical Cytology Brushes

Report – DV Test report for the Triple Needle Brush Packaging

Document No.:	[redacted]	Revision (b) (4)
Document Title:	Package Testing Protocol for Hobbs Medical Cytology Brushes	Effective [redacted]
Owner:		
Author:	(b) (4), (b) (6) [redacted]	

Package Testing Protocol for Hobbs Medical Cytology Brushes

Table of Contents

Document No.:	[redacted]	Revision	(b) (4) [redacted]
Document Title:	Package Testing Protocol for Hobbs Medical Cytology Brushes	Effective	
Owner:			
Author:	(b) (4), (b) (6) [redacted]		

1.0 PURPOSE

The purpose of this protocol is to define the testing and acceptance criteria needed to demonstrate that the packaging of Hobbs Medical cytology brushes will adequately protect its contents from physical/functional damage and will maintain a sterile barrier, at baseline after 2 time ethylene oxide (EtO) sterilization (Time=0), after simulated shipping & handling conditions (via environmental and distribution simulation testing) and after the defined shelf-life time points (via accelerated aging).

This protocol will only address the packaging components of the Hobbs Medical cytology brushes. The product testing will be covered under separate protocol(s).

2.0 DEFINITIONS / ACRONYMS / ABBREVIATIONS

HMI	Hobbs Medical Inc
DDL	Dynamic Distribution Laboratories
IFU	Instructions for Use

3.0 REFERENCES

(b) (4) [redacted]

(b) (4) Testing

(b) (4) Testing

(b) (4) Testing

(b) (4) Testing

10.0 ACCEPTANCE CRITERIA

10.1 Acceptance criteria for superDimension inspections

(b) (4)

Table 3 – Inspections of packaging after distribution simulation and after accelerated aging

10.2 Acceptance criteria for DDL package testing

10.2.1 It shall be shown with 80% confidence that 90% of sample unit package seals will meet the seal integrity requirements called out in ASTM-F2096-04.

10.2.2 It shall be shown with 80% confidence that 90% of sample unit package seals at baseline and time zero will meet the seal strength of 0.75 lbf per inch of seal length minimum and 3 lbf maximum average peel strength per ASTM F88-09 seal pull. It shall be shown that after 2X sterilization, aging and distribution simulation that the pouches will maintain their visual integrity and pass the bubble leak testing as well as a seal strength of 0.75 lbf per inch of seal length minimum and 3 lbf maximum average peel strength per inch of seal length per ASTM F-88 seal pull.

(b) (4)

11.0 TEST FORMS

The following completed test forms will be included in the final report

DDL provided documentation

- Distribution Cycle report
- Environmental Report for Accelerated Aged Devices
- Sterile barrier integrity results will be reported by DDL on their internal report templates.

superDimension provided documentation

- Visual Inspection of all elements in Table 3 are listed in Appendix A

Appendix A

Time point/Test Group (circle one) 1) Baseline 2) Time = 0 years with distribution testing 3) T = 1 year accelerated aging 4) T=5 year accelerated aging			
Lot Number _____			
Specification Requirement Document (b) (4) [redacted] (b) (4) [redacted]			
Product pouch			
1.	P□ F□	P□ F□	P□ F□
2.	P□ F□	P□ F□	P□ F□
3.	P□ F□	P□ F□	P□ F□
4.	P□ F□	P□ F□	P□ F□
5.	P□ F□	P□ F□	P□ F□
6.	P□ F□	P□ F□	P□ F□
7.	P□ F□	P□ F□	P□ F□
8.	P□ F□	P□ F□	P□ F□
9.	P□ F□	P□ F□	P□ F□
10.	P□ F□	P□ F□	P□ F□
11.	P□ F□	P□ F□	P□ F□
12.	P□ F□	P□ F□	P□ F□
13.	P□ F□	P□ F□	P□ F□
14.	P□ F□	P□ F□	P□ F□
15.	P□ F□	P□ F□	P□ F□
16.	P□ F□	P□ F□	P□ F□
17.	P□ F□	P□ F□	P□ F□
18.	P□ F□	P□ F□	P□ F□
19.	P□ F□	P□ F□	P□ F□
20.	P□ F□	P□ F□	P□ F□
Product box			
1.	P□ F□	P□ F□	P□ F□
2.	P□ F□	P□ F□	P□ F□
Tested By:			
Date Tested:			
Date Reviewed:			

		Revision (b) (4)
Document Title:	Report – DV Test report for the Triple Needle Brush Packaging	Effectiv
Owner:	Research and Development	Page 1 of 7
Author:	(b) (4), (b) (6)	

Design Verification Test Report for the Triple Needle Brush Packaging

Table of Contents

1.0 PURPOSE

The purpose of this report is to document all the actions performed listed in the protocol to validate the Triple Needle Brush packaging for production use at Hobbs Medical.

2.0 REFERENCES

(b) (4)

3.0 TEST DATA

The package design for the cytology brush family is a typical flexible peel pouch. This pouch is Tyvek on one side and a laminated PET (Polyethylene terephthalate) / LDPE (Low Density Polyethylene) film on the other side. The Tyvek pouch has three sides sealed at the factory and one side sealed at the manufacturer. The pouch is wide enough and long enough to accommodate the finished product. The shelf carton is designed to open on the end to allow access to the contents of the product box. The shelf carton and shipping box must protect the product from damage during distribution.

There are essentially two sets of data in this test report:
1) Bubble leak and seal strength testing performed by Dynamic Distribution Labs (DDL)
2) Packaging inspection based on the design specification – performed by superDimension personnel

All test data is attached via embedded documents in appendix A
The DDL reports are below.

Below is a table from the protocol ( ) with all the test groups and the tests to be performed with the stated sample sizes.

(b) (4)

Table 1: Test Groups and Number of Samples Required per Test

Test	Group 1 Baseline: (2X EtO)	Group 2 Environmental & Distribution Simulation (2X EtO + DS)	Group 3 1 yr Accelerated Age (2X EtO)	Group 4 5 yr Accelerated Age (2X EtO)
Bubble Leak ASTM F2096-04	20	20	20	20
Seal strength testing ASTM F88-07	20	20	20	20
TOTAL	40	40	40	40

Listed below are the acceptance criteria for each test for the product packaging design.

(b) (4)

(b) (4)

Figure 1 – Example of labeled shipping boxes for DDL testing

There are four test groups:
Group 1) Baseline / Control group at time zero was tested post 2X sterilization
Group 2) Environmental control and distribution group was exposed to the 2X sterilization, environmental conditioning and subsequent distribution simulation test procedure
Group 3) 1 year accelerated aging was exposed to 2X sterilization and accelerated aging at 55°C for 38 days at <20%RH
Group 4) 5 year accelerated aging was exposed to 2X sterilization and accelerated aging at 55°C for 186 days at <20%RH. At the time of this report the 5 year product was still aging. The results from the 5 year shelf life packaging test will be added to this report as the results become available.

Group 1: Baseline/Control (T=0 years)
Time zero product samples were tested for visual, seal strength and bubble leak testing. Summary results can be found in table 3 below and raw data can be found in the embedded DDL report in Appendix A.

Group 2: Environmental conditioning and Distribution Simulation
The environmental conditioning and distribution test group was tested for visual, seal strength and bubble leak testing. Summary results can be found in table 3 below and raw data can be found in the embedded DDL report in Appendix A.

Group 3: Accelerated aging
Time = 1 year accelerated aging parts were removed from the environmental chamber on the 38th day. They were tested for visual, seal strength and bubble leak testing. Summary results can be found in table 3 below and raw data can be found in the embedded DDL report in Appendix A.

The data sheet(s) for the visual inspection performed at sDI is summarized below and raw data can be found in Appendix A.

Table 3: Summary results of packaging testing.

(b) (4)

(b) (4)

4.0 ANALYSIS OF RESULTS

The results of the package testing showed that all of the test criteria were met. There were no failures for visual inspection of the box or pouch, damage, leaks, or peel strength. This data suggests that the pouch and box are satisfactory packaging materials under the current production processes for up to one year.

(b) (4)

(b) (4)

6.0 CONCLUSION

6.1 The Product packaging including Pouch (Hobbs Medical part number COM-0655) and the product Box (Hobbs Medical part number COM-0688) are confirmed as acceptable for Hobbs ongoing production use of the cytology brush family of tools manufactured for superDimension, including the triple needle tipped cytology brush.

6.2 The shipping Box (superDimension Part Number 1584-1) is an acceptable shipper for Hobbs cytology brushes when packaged 2 shelf cartons per shipper.

6.3 The data for the pouch at time zero, i.e. after 2X sterilization resulted in pouch integrity values which meet all described acceptance criteria.

6.4 The pouches after being subjected to environmental conditioning and distribution simulation meet all required acceptance criteria.

6.5 The pouches exposed to one-year accelerated aging per the condition stated meet all required acceptance criteria.

6.6 The data from the five year accelerated aging group of devices will be reported in a subsequent revision of this when the data becomes available.

(b) (4)

Attachment 9

Design Verification Testing

Contents:

(b) (4) Biocompatibility Test Report of Triple Needle Tipped Brush Biopsy Tool

Document No.:	[redacted]	Revisio	(b) (4) [redacted]
Document Title:	Biocompatibility Test Report of Triple Needle Tipped Brush Biopsy Tool	Effecti	
Owner:	R & D	Page 1 of 6	
Author:	(b) (4), (b) (6) [redacted]		

Biocompatibility Test Report of Triple Needle Tipped Brush Biopsy Tool

Table of Contents

Document No.:	[redacted]	Revision: (b) (4) [redacted]
Document Title:	Biocompatibility Test Report of Triple Needle Tipped Brush Biopsy Tool	Effective: [redacted]
Owner:	R & D	Page 2 of 6
Author:	(b) (4), (b) (6) [redacted]	

1.0 PURPOSE

The purpose of this report is to demonstrate the biocompatibility of the materials and processing used to manufacture the superDimension (sD) Triple Needle-Tipped Cytology Brush (TNB). This biopsy tool includes sD part numbers SDTNB1000 & SDTNB1500. Biocompatibility is based on standards referenced in Section 3.0.

2.0 DEFINITIONS / ACRONYMS / ABBREVIATIONS

sD: superDimension
EWC: Extended Working Channel
HMI: Hobbs Medical, Inc.
TNB: Triple Needle Tipped Brush Biopsy Tool

3.0 REFERENCES

(b) (4) [redacted]

4.0 MATERIALS OF CONSTRUCTION

Refer to the Table below for identification of the materials qualified per this test report. See the Test Article Section of Test Protoco(b) (4) r a list of raw materials. (b) (4) [redacted]

(b) (4) [redacted]

(b) (4) Testing, (b) (4) Materials, (b) (4) Protocols

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Attachment 10

Design Verification Testing

Contents:

(b) (4) Design Verification Test Protocol for Triple Needle Cytology Brush

Design Verification Test Report, Triple Needle Cytology Brush

Design Verification Test Protocol for Triple Needle Brush Supplemental Testing

(b) (4) Design Verification Test Report for Supplemental Testing on Needle Brush (Bristle Condition and Aspiration Port)

Design Verification Test Protocol for Triple Needle Brush

Table of Contents

1.0 PURPOSE

The purpose of this protocol is to define the testing and acceptance criteria needed to demonstrate that the Triple Needle Brush meets required functionality specification per specification requirements document [A5].

This protocol covers the verification tests for Triple Needle Brush, Hobbs Medical P/N's SDTNB1000 and SDTNB1500.

This protocol covers the functional tests to be performed on the test samples after conditioning processes such as EtO sterilization, distribution simulation and accelerated aging.

Other elements of the design specification will be verified under separate protocols and reports (Packaging and sterilization).

2.0 DEFINITIONS / ACRONYMS / ABBREVIATIONS

HMI	Hobbs Medical Inc.
TNB	Triple Needle Brush
CR	Customer Requirements
DI	Design Input
DC	Delivery Cartridge
ENB	Electromagnetic Navigation Bronchoscopy
EWC	Extended Working Channel
ID	Identification
LG	Locatable Guide
N	Newton – MKS force unit
N/A	No applicable requirements in the specific section
P/N	Part Number
SU	Single Use
Target	Designated area in the lung (which the physician selects during planning).
TBD	To Be Defined

3.0 REFERENCES

(b) (4)

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(b) (4)

(b) (4)

11.0 TEST PROTOCOL TRACEABILITY

See table above.

12.0 TEST FORMS

Test forms are in each of the referenced test methods.

		Revisio (b) (4)
Document Title:	Design Verification Test Report, Triple Needle Cytology Brush	Effecti
Owner:	Research and Development	Page 1 of 16
Author:	(b) (4), (b) (6)	

Design Verification Test Report, Triple Needle Cytology Brush

Table of Contents

1.0 PURPOSE

1.1 The purpose of this report is to summarize the results of the design verification data, tested pe (b) (4) demonstrate conformance of the design verification samples to the design verification specifications p (b) (4)

2.0 REFERENCES

(b) (4)

(b) (4) Testing

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(b) (4) Testing

	[redacted]	Revision	(b) (4) [redacted]
Document Title:	Design Verification Test Protocol for Triple Needle Brush - Supplemental Testing	Effective	
Owner:			
Author:	(b) (4), (b) (6) [redacted]		

1.0 PURPOSE

The purpose of this protocol is to define the testing and acceptance criteria needed to demonstrate that the Triple Needle Brush meets the following three specifications per specification requirements document

(b) (4) Testing [redacted]

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Design Verification Test Report for Supplemental Testing on Needle Brush (Bristle Condition and Aspiration Port)

Table of Contents

1.0 PURPOSE

The purpose of this report is to report the results of the supplemental testing and to demonstrate that the Triple Needle Brush meets the following three specifications per specification requirements documents.

(b) (4) Testing

(b) (4) Testing

(b) (4) Testing

4.0 ANALYSIS OF RESULTS

(b) (4) Testing

(b) (4)

(b) (4)

5.0 PROTOCOL DISCREPANCIES

There were no protocol discrepancies.

6.0 CONCLUSION

(b) (4)

All device subassemblies tested met specification

With an 80% confidence and 85% reliability level, acceptance was demonstrated with 20 parts and 1failure.

All device subassemblies tested met acceptance criteria defined in test protocol

Summary

With an 80% confide
design specifications

Barlow, Lenny *

From: Barlow, Lenny *
Sent: Thursday, November 07, 2013 3:51 PM
To: 'Kristen.Swanson@covidien.com'
Cc: DCCLetters
Subject: k130357 Correspondence
Attachments: k130357.pdf

COVER SHEET MEMORANDUM

Food and Drug Administration
Office of Device Evaluation &
Office of In Vitro Diagnostics and
Radiological Health

From: Reviewer Name Sunny Park

Subject: 510(k) Number K130357

To: The Record

Please list CTS decision code: SE - Substantially Equivalent

☐ Refused to Accept (Note: this is considered the first review cycle. See screening checklist.)

☐ Hold (Additional Information or Telephone Hold)

☒ Final Decision (SE, SE with Limitations, NSE (select code below), Withdrawn, etc.)

Please complete the following for a final clearance decision (i.e, SE, SE with Limitations, etc.)	YES	NO
Indications for Use Page *(Attach IFU)*	X	
510(k) Summary or 510(k) Statement *(Attach Summary or Statement)*	X	
Truthful and Accurate Statement *(Must be present for a Final Decision)*	X	
Is the device Class III?		X
Does firm reference standards? (If yes, please attach Form 3654.)	X	
Is this a combination product?		X
Is this a reprocessed single use device? (See Guidance for Industry and FDA Staff - MDUFMA - Validation Data in 510(k)s for Reprocessed Single-Use Medical Devices.)		X
Is this device intended for pediatric use only?		X
Is this a prescription device? (If both prescription & OTC, check both boxes.)	X	
Is clinical data necessary to support the review of this 510(k)?		X
For United States based clinical studies only, did the application include a completed Form FDA 3674, Certification with Requirements of ClinicalTrials.gov Data Bank? (If study was conducted in the United States and Form FDA 3674 was not included or was incomplete, then applicant must be contacted to obtain completed form.)		
Does this device include an Animal Tissue Source?		X
All Pediatric Patients age <= 21		
Neonate/Newborn (Birth to 28 days)		
Infant (29 days to < 2 years)		
Child (2 years to <12 years)		
Adolescent (12 years to <18 years)		
Transitional Adolescent A (18 years to <21 years); Special considerations are being given to this group, different from adults age >= 21 (different device design or tesating, different protocol procedures, etc.)		
Transitional Adolescent B (18 years to <21 years); No special considerations compared to adults >= 21 years)		

Nanotechnology		X
Is this device subject to the Tracking Regulation? (Medical Device Tracking Guidance)		X

Regulation Number: 21 CFR 874.4680

Class: II

Product Code: BTG

Additional Product Codes:

Digital Signature Concurrence Table
(Not all signatures may be required)

Branch Chief Sign-Off	Srinivas Nandkumar -S 2013.11.05 10:06:46 -05'00'
Division Sign-Off	Eric A. Mann -S 2013.11.06 10:42:13 -05'00'

K130357/S001

COVIDIEN

September 27, 2013

Dr. Sunny Park
U.S. Food and Drug Administration
Center for Devices and Radiological Heath
Document Mail Center – WO66-G609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

Re: K130357 Covidien superTrax® Triple Needle-Tipped Cytology Brush
Request for Additional Information

Dear Dr. Park,

In response to FDA's request for additional information on the 510(k) application K130357 (letter dated April 10, 2013) for the superTrax Triple Needle-Tipped Cytology Brush, superDimension Inc. is supplying the following explanations and data in support of the safety and performance of this device. The meeting minutes from the April 22, 2013 discussion between FDA and Covidien are also included as an addendum to this cover. The included eCopy is an exact duplicate of the paper copy.

Please note that, in addition to answering the questions, the product name has been changed slightly for branding reasons. The name "superTrax Triple Needle-Tipped Cytology Brush" has been changed to "SuperDimension Triple Needle Cytology Brush". This does not impact any technical information on the product and is reflected in the included draft labeling. Included in the labeling attachment is a revised 510(k) summary reflecting the name change as well as the revised Indications for Use.

Covidien (d/b/a superDimension Inc.) believes this data, when combined with the information supplied in the original 510(k) submission, justifies finding the Triple Needle Cytology Brush substantially equivalent to the ConMed Needle-Tip Cytology Brush and the Hobbs Medical Cytology Brush.

All information contained within this response is considered confidential. If you have any questions or require additional information to facilitate your review, Kristen Swanson can be reached at (763) 210-4062 or via email at Kristen.Swanson@covidien.com. Alternatively, you may contact me at (763) 210-4091 or via email at Deborah.Fleetham@covidien.com.

Sincerely,

Deborah Fleetham

Deborah Fleetham
Manager, Regulatory Affairs

Addendum: Meeting minutes from April 22, 2013

Covidien llc **161 Cheshire Lane Suite 100 Minneapolis, MN U.S.A. 55441** **800-387-9016 (T) 763-210-4098 (F)**

COVIDIEN

September 27, 2013

Dr. Sunny Park
U.S. Food and Drug Administration
Center for Devices and Radiological Heath
Document Mail Center – WO66-G609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

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All information contained within this response is considered confidential. If you have any questions or require additional information to facilitate your review, Kristen Swanson can be reached at (763) 210-4062 or via email at Kristen.Swanson@covidien.com. Alternatively, you may contact me at (763) 210-4091 or via email at Deborah.Fleetham@covidien.com.

Sincerely,

Deborah Fleetham

Deborah Fleetham
Manager, Regulatory Affairs

Addendum: Meeting minutes from April 22, 2013

Covidien llc
161 Cheshire Lane Suite 100
Minneapolis, MN U.S.A.
55441
800-387-9016 (T)
763-210-4098 (F)

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(b) (4)

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DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

CDRH PREMARKET REVIEW SUBMISSION COVER SHEET

Form Approval
OMB No. 0910-0120
Expiration Date: December 31, 2013
See PRA Statement on page 5.

Date of Submission	User Fee Payment ID Number	FDA Submission Document Number *(if known)*
September 27, 2013		K130357

SECTION A TYPE OF SUBMISSION

PMA	PMA & HDE Supplement	PDP	510(k)	Request for Feedback
☐ Original Submission	☐ Regular (180 day)	☐ Original PDP	☐ Original Submission:	☐ Pre-Submission
☐ Premarket Report	☐ Special	☐ Notice of Completion	☐ Traditional	☐ Informational Meeting
☐ Modular Submission	☐ Panel Track (PMA Only)	☐ Amendment to PDP	☐ Special	☐ Submision Issue Meeting
☐ Amendment	☐ 30-day Supplement		☐ Abbreviated (Complete section I, Page 5)	☐ Day 100 Meeting
☐ Report	☐ 30-day Notice		☒ Additional Information	☐ Agreement Meeting
☐ Report Amendment	☐ 135-day Supplement		☐ Third Party	☐ Determination Meeting
☐ Licensing Agreement	☐ Real-time Review			☐ Study Risk Determination
	☐ Amendment to PMA & HDE Supplement			☐ Other *(specify):*
	☐ Other			

IDE	Humanitarian Device Exemption (HDE)	Class II Exemption Petition	Evaluation of Automatic Class III Designation (De Novo)	Other Submission
☐ Original Submission	☐ Original Submission	☐ Original Submission	☐ Original Submission	☐ 513(g)
☐ Amendment	☐ Amendment	☐ Additional Information	☐ Additional Information	☐ Other *(describe submission):*
☐ Supplement	☐ Supplement			
	☐ Report			
	☐ Report Amendment			

Have you used or cited Standards in your submission? ☒ Yes ☐ No *(If Yes, please complete Section I, Page 5)*

SECTION B SUBMITTER, APPLICANT OR SPONSOR

Company / Institution Name	Establishment Registration Number *(if known)*		
Covidien llc	3004962788		
Division Name *(if applicable)*	**Phone Number *(including area code)***		
Interventional Lung Solutions, formerly superDimension Inc.	763-210-4091		
Street Address	**FAX Number *(including area code)***		
161 Cheshire Lane Suite 100	763-210-4098		
City	**State / Province**	**ZIP/Postal Code**	**Country**
Minneapolis	Minnesota	55441	U.S.A.
Contact Name			
Deborah Fleetham			
Contact Title	**Contact E-mail Address**		
Manager Regulatory Affairs	deborah.fleetham@covidien.com		

SECTION C APPLICATION CORRESPONDENT (e.g., consultant, if different from above)

Company / Institution Name			
Division Name *(if applicable)*	**Phone Number *(including area code)***		
Street Address	**FAX Number *(including area code)***		
161 Cheshire Lane Suite 100	763-210-4098		
City	**State / Province**	**ZIP Code**	**Country**
Minneapolis	Minnesota	55441	U.S.A.
Contact Name			
Kristen Swanson			
Contact Title	**Contact E-mail Address**		
Regulatory Consultant	kristen.swanson@covidien.com		

PSC Publishing Services (301) 443-6740 EF

SECTION D1 REASON FOR APPLICATION - PMA, PDP, OR HDE

- ☐ New Device
- ☐ Withdrawal
- ☐ Additional or Expanded Indications
- ☐ Request for Extension
- ☐ Post-approval Study Protocol
- ☐ Request for Applicant Hold
- ☐ Request for Removal of Applicant Hold
- ☐ Request to Remove or Add Manufacturing Site

- ☐ Change in design, component, or specification:
  - ☐ Software / Hardware
  - ☐ Color Additive
  - ☐ Material
  - ☐ Specifications
  - ☐ Other *(specify below)*

- ☐ Location change:
  - ☐ Manufacturer
  - ☐ Sterilizer
  - ☐ Packager

- ☐ Process change:
  - ☐ Manufacturing ☐ Packaging
  - ☐ Sterilization
  - ☐ Other *(specify below)*

- ☐ Labeling change:
  - ☐ Indications
  - ☐ Instructions
  - ☐ Performance Characteristics
  - ☐ Shelf Life
  - ☐ Trade Name
  - ☐ Other *(specify below)*

- ☐ Report Submission:
  - ☐ Annual or Periodic
  - ☐ Post-approval Study
  - ☐ Adverse Reaction
  - ☐ Device Defect
  - ☐ Amendment

- ☐ Response to FDA correspondence:

- ☐ Change in Ownership
- ☐ Change in Correspondent
- ☐ Change of Applicant Address

- ☐ Other Reason *(specify):*

SECTION D2 REASON FOR APPLICATION - IDE

- ☐ New Device
- ☐ New Indication
- ☐ Addition of Institution
- ☐ Expansion / Extension of Study
- ☐ IRB Certification
- ☐ Termination of Study
- ☐ Withdrawal of Application
- ☐ Unanticipated Adverse Effect
- ☐ Notification of Emergency Use
- ☐ Compassionate Use Request
- ☐ Treatment IDE
- ☐ Continued Access

- ☐ Change in:
  - ☐ Correspondent / Applicant
  - ☐ Design / Device
  - ☐ Informed Consent
  - ☐ Manufacturer
  - ☐ Manufacturing Process
  - ☐ Protocol - Feasibility
  - ☐ Protocol - Other
  - ☐ Sponsor

- ☐ Report submission:
  - ☐ Current Investigator
  - ☐ Annual Progress Report
  - ☐ Site Waiver Report
  - ☐ Final

- ☐ Response to FDA Letter Concerning:
  - ☐ Conditional Approval
  - ☐ Deemed Approved
  - ☐ Deficient Final Report
  - ☐ Deficient Progress Report
  - ☐ Deficient Investigator Report
  - ☐ Disapproval
  - ☐ Request Extension of Time to Respond to FDA
  - ☐ Request Meeting
  - ☐ Request Hearing

- ☐ Other Reason *(specify):*

SECTION D3 REASON FOR SUBMISSION - 510(k)

- ☐ New Device
- ☐ Additional or Expanded Indications
- ☐ Change in Technology

- ☒ Other Reason *(specify):*

Response to a request for additional information

SECTION E ADDITIONAL INFORMATION ON 510(K) SUBMISSIONS

Product codes of devices to which substantial equivalence is claimed

1		2		3		4	
5		6		7		8	

Summary of, or statement concerning, safety and effectiveness information

☐ 510 (k) summary attached
☐ 510 (k) statement

Information on devices to which substantial equivalence is claimed *(if known)*

	510(k) Number		*Trade or Proprietary or Model Name*		*Manufacturer*
1		1		1	
2		2		2	
3		3		3	
4		4		4	
5		5		5	
6		6		6	

SECTION F PRODUCT INFORMATION - APPLICATION TO ALL APPLICATIONS

Common or usual name or classification name

	Trade or Proprietary or Model Name for This Device		Model Number
1		1	
2		2	
3		3	
4		4	
5		5	

FDA document numbers of all prior related submissions *(regardless of outcome)*

1	2	3	4	5	6
7	8	9	10	11	12

Data Included in Submission

☒ Laboratory Testing ☒ Animal Trials ☐ Human Trials

SECTION G PRODUCT CLASSIFICATION - APPLICATION TO ALL APPLICATIONS

Product Code	C.F.R. Section *(if applicable)*	Device Class
BTG	874.4680	☐ Class I ☒ Class II ☐ Class III ☐ Unclassified

Classification Panel

Ear, Nose, and Throat

Indications *(from labeling)*

To be utilized through a flexible endoscope or the superDimension system by physicians who are trained in endoscopic techniques for retrieving specimens from patients with endobronchial lesions, peripheral lung nodules, or lung masses.

Note: **Submission of the information entered in Section H does not affect the need to submit device establishment registration.**

FDA Document Number *(if known)*

SECTION H — MANUFACTURING / PACKAGING / STERILIZATION SITES RELATING TO A SUBMISSION

☐ Original ☐ Add ☐ Delete	Facility Establishment Identifier (FEI) Number	☐ Manufacturer ☐ Contract Sterilizer ☐ Contract Manufacturer ☐ Repackager / Relabeler
Company / Institution Name		Establishment Registration Number
Division Name *(if applicable)*		Phone Number *(including area code)*
Street Address		FAX Number *(including area code)*
City		State / Province | ZIP Code | Country
Contact Name	Contact Title	Contact E-mail Address

☐ Original ☐ Add ☐ Delete	Facility Establishment Identifier (FEI) Number	☐ Manufacturer ☐ Contract Sterilizer ☐ Contract Manufacturer ☐ Repackager / Relabeler
Company / Institution Name		Establishment Registration Number
Division Name *(if applicable)*		Phone Number *(including area code)*
Street Address		FAX Number *(including area code)*
City		State / Province | ZIP Code | Country
Contact Name	Contact Title	Contact E-mail Address

☐ Original ☐ Add ☐ Delete	Facility Establishment Identifier (FEI) Number	☐ Manufacturer ☐ Contract Sterilizer ☐ Contract Manufacturer ☐ Repackager / Relabeler
Company / Institution Name		Establishment Registration Number
Division Name *(if applicable)*		Phone Number *(including area code)*
Street Address		FAX Number *(including area code)*
City		State / Province | ZIP Code | Country
Contact Name	Contact Title	Contact E-mail Address

SECTION I UTILIZATION OF STANDARDS

Note: Complete this section if your application or submission cites standards or includes a *"Declaration of Conformity to a Recognized Standard"* statement.

	Standards No.	Standards Organization	Standards Title	Version	Date
1	10555-1	ISO	Sterile, single-use intravascular catheters Part 1: General Requirements	2009	May 2009
2	Standards No.	Standards Organization	Standards Title	Version	Date
3	Standards No.	Standards Organization	Standards Title	Version	Date
4	Standards No.	Standards Organization	Standards Title	Version	Date
5	Standards No.	Standards Organization	Standards Title	Version	Date
6	Standards No.	Standards Organization	Standards Title	Version	Date
7	Standards No.	Standards Organization	Standards Title	Version	Date

Please include any additional standards to be cited on a separate page.

This section applies only to requirements of the Paperwork Reduction Act of 1995.

DO NOT SEND YOUR COMPLETED FORM TO THE PRA STAFF ADDRESS BELOW.

The burden time for this collection of information is estimated to average 0.5 hour per response, including the time to review instructions, search existing data sources, gather and maintain the data needed and complete and review the collection of information. Send comments regarding this burden estimate or any other aspect of this information collection, including suggestions for reducing this burden, to:

Department of Health and Human Services
Food and Drug Administration
Office of Chief Information Officer
Paperwork Reduction Act (PRA) Staff
1350 Piccard Drive, Room 400
Rockville, MD 20850

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

(b) (4) Design

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ATTACHMENT 1

GLP Animal Study Report

(b) (4) –Safety Evaluation of the Triple Needle Cytology Brush in a Porcine Model Study Report

Document No.:	[redacted]	Revision:	(b) (4) [redacted]
Document Title:	Safety Evalution of the Triple Needle Cytology Brush in a Porcine Model	Effective:	
Owner:	R&D Engineering	Page 1 of 309	
Author:	(b) (4), (b) (6) [redacted]		

Safety Evaluation of the Triple Needle Cytology Brush in a Porcine Model Study Report

Table of Contents

1.0 PURPOSE

The purpose of the report is to evaluate the safety of the Triple Needle-Tipped Cytology Brush in a porcine model undergoing a lung biopsy endobronchial procedure and to provide clinical evidence of the safety of this product to satisfy regulatory submission requirements.

This study was conducted in collaboration with American Preclinical Services (APS) under the APS stud(b) (4) [redacted] testing was performed at the APS facility by study physicians who are superDimension users. The study was performed in accordance to Good Laboratory Practices (GLP) for medical devices.

The data collection and analysis was completed by APS. The evaluation of the test results against the acceptance criteria, and the collection of the physician's assessments, was performed by Covidien.

2.0 SCOPE

2.1 The study applies to the following Triple Needle-Tipped Cytology Brush model numbers:

- **2.1.1** SDTNB1000
- **2.1.2** SDTNB1500

2.2 The study was conducted using the SDTNB 1500 model considered to be the most challenging from a safety perspective due to having a longer brush and wider tip spread. The SDTNB 1500 is 0.5 cm longer than the SDTNB1000 when fully deployed.

3.0 DEFINITIONS / ACRONYMS / ABBREVIATIONS

TNB	SuperDimension Triple Needle-Tipped Cytology Brush
SNB	Conmed (single) Needle Tipped Brush
APS	American Preclinical Services
SD	SuperDimension
GLP	Good Laboratory Practices per 21 CFR Part 58 (FDA)
AAALAC	American Association for the Advancement of Laboratory Animal Care
CFR	Code of Federal Regulations
PNMTHX	Pneumothorax

4.0 REFERENCES

(b) (4) [redacted] Safety Evaluation of the Triple Needle Cytology Brush in a Porcine Model

5.0 SUMMARY OF TESTING ACTIVITIES

(b) (4) [redacted]

6.0 STUDY ENVIRONMENT

The animal study was done at the American Preclinical Services (APS) facility. APS is an AAALAC accredited institution which follows pertinent accepted standards for laboratory animal care. The details of the facility are included in the attached GLP report, see Appendix A.

7.0 EQUIPMENT / MATERIALS / TOOLS

All of the test equipment, materials, and tools are included in the attached GLP report, see Appendix A.

8.0 TEST ARTICLES

The test devices were:

- TNB – Part Number: SDTNB1500 (test article)
- SNB – Part Number: ConMed PN NB-120 (control article 01 [predicate device])
- superTrax Forceps – Part Number: SDBF1000 (control article 02 [included as reference])

While the superTrax Forceps are not a predicate device for the TNB, this was included to provide a frame of reference for a standard biopsy tool in order to evaluate the tissue damage.

9.0 SAMPLE SIZE DETERMINATION

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10.0 TEST METHOD

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11.0 DATA / RESULTS

All in-life raw data is retained in the archives of APS according to federal regulations for GLP studies.

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In summary:

- The incidence and severity of bleeding at biopsy sites both intra-operatively and at gross necropsy was lower with the TNB treated sites in comparison to the SNB treated sites, and both devices were lower than the forceps. There was no statistically significant difference between TNB and SNB based on incidence or severity of bleeding.
- There was no statistically significant difference between the TNB + forceps treated lungs and SNB + forceps treated lungs based on incidence and severity of pneumothorax in the radiological evaluation at each of the three post-treatment time points. None of the animals exhibited pneumothorax symptoms in their physical exam.
- Trauma / tissue damage was statistically equivalent for the TNB and SNB treated sites and was considered clinically insignificant and typical of biopsy procedures. Overall, use of the forceps introduced increased amounts of trauma / tissue damage at the treatment sites when compared to the use of either the TNB or SNB.
- Tissue sampling showed statistical significance was equivalent for absolute nucleated cell counts between the TNB and SNB with a trend towards superiority of the TNB. The overall median absolute nucleated cell count for TNB was 2.9 times greater than for the SNB.
- Overall animal health findings were considered common observation in laboratory animals following an anesthetic and surgical procedure and were not attributed to the test or control devices.
- The study physicians had no concerns with the safety of the TNB.

13.0 PROTOCOL DISCREPANCIES

There were no protocol discrepancies or deviations.

14.0 CONCLUSION

The results shown by the study report provided by APS report shows the acceptance criteria for the study has been met.

In conclusion, based on the scope of this study, the superDimension Triple Needle-Tipped Cytology Brush (TNB) demonstrated substantially equivalent safety profile when compared to the ConMed Single Needle-Tip Cytology Brush (SNB).

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ATTACHMENT 2
ANIMAL STUDY LITERATURE REFERENCES

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Efficacy of Bronchial Brush Cytology and Bronchial Washings in Diagnosis of Non Neoplastic and Neoplastic Bronchopulmonary Lesions

Neoplastik ve Nonneoplastik Bronkopulmoner Lezyonların Tanısında Bronş Fırçalama ve Yıkama Materyallerinin Etkinliği

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ABSTRACT

Objective: The present study is based on the cytologic evaluation of bronchial brushings for the diagnosis of non neoplastic and neoplastic bronchopulmonary lesions and relation of the cytologic findings with clinical diagnosis and histopathologic examination wherever possible.

Material and Method: 35 symptomatic patients were selected on whom bronchoscopy was done. Bronchial brushing was performed using straight brushes and bronchial washing specimens were collected after brushing samples. Smears were stained by PAP, H&E, and Giemsa in all the cases while PAS and Ziehl Neelsen stainings were done in selected cases. Endobronchial biopsy was performed using a flexible long biopsy forceps.

Results: The age of the patients varied from 18 to 88 years, and the male:female ratio was 3.3:1. Carcinoma was diagnosed in 21 (60%) out of total 35 cases on bronchial biopsy and the remaining 14 cases (40%) showed inflammatory, tuberculous or no significant pathology. Bronchial washing showed 10 true positive, 10 true negative, 4 false positive and 11 false negative cases whereas bronchial brushing showed 17 true positive, 12 true negative, 2 false positive and 4 false negative cases as confirmed on biopsy. Bronchial brushing showed good sensitivity (80.9%) and specificity (85.7%) compared to bronchial washing which had sensitivity of 47.6% and specificity of 71.4%.

Conclusion: These findings attempted to confirm the concept that pulmonary cytology has improved to the point that its sensitivity is high enough to justify its use as a definitive diagnostic tool in those cases in which tissue diagnosis is not possible.

Key Words: Cytology, Pulmonary neoplasms, Pulmonary abscess, Tuberculosis, Chronic bronchitis

ÖZ

Amaç: Neoplastik ve non-neoplastik akciğer lezyonlarında bronş fırçalama materyalinin sitolojik değerlendirme sonuçlarını klinik tanı ve histopatolojik inceleme sonuçları ile karşılaştırmak.

Gereç ve Yöntem: Bronkoskopi yapılan 35 semptomatik olgu değerlendirmeye alındı. Rutin bronş fırçalaması ve ardından bronş yıkama sıvısı alındı. Yaymalar PAP, H&E ve Giemsa ile, gereken olgularda ek olarak PAS ve Ziehl Neelsen ile boyandı. Ayrıca, biyopsi forsepsi ile endobronşial biyopsi alındı.

Bulgular: Olguların yaşı 18-88 arasında değişiyordu ve erkek:kadın oranı 3.3:1'di. 35 olgunun 21'inde (%60) karsinom saptanırken, diğer 14 olguda (%40) enflamatuvar lezyon, tüberküloz veya patoloji olmadığı saptandı. Bronş iğne biyopsisi ile değerlendirildiğinde bronş yıkama materyali 10 gerçek pozitif, 10 gerçek negatif, 4 yanlış pozitif, 11 yanlış negatif sonuç verirken, bronş fırçalama materyali 17 gerçek pozitif, 12 gerçek negatif, 2 yanlış pozitif, 4 yanlış negative sonuç verdi. Bronş fırçalaması iyi duyarlılık (%80,9) ve özgüllük (%85,7) gösterirken, bronş yıkamasında duyarlılık %47,6 ve özgüllük %71,4 düzeyinde kaldı.

Sonuç: Sonuçlar, doku tanısı yetersiz olduğunda akciğer sitolojisinin tanısal olarak kullanılabilecek duyarlılığa sahip olduğu görüşünü desteklemektedir

Anahtar Sözcükler: Sitoloji, Akciğer tümörleri, Akciğer apsesi, Tüberküloz, Kronik bronşit

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INTRODUCTION

The flexible fibreoptic bronchoscope enables several investigations to be carried out but selective bronchial brushing seems to be the most rewarding as the results obtained by brushing are often superior to those obtained by bronchial washings, biopsy or sputum examination, especially for lesions located distal to segmental bronchi. Studies done using bronchial brushing for cytodiagnosis of lung cancer have emphasised its high accuracy rate in the evaluation of neoplastic and non neoplastic pulmonary lesions (1-6). The present study is based on the cytologic evaluation of bronchial brushings for the diagnosis of non neoplastic and neoplastic bronchopulmonary lesions and correlates the cytologic findings with the clinical diagnosis and histopathologic examination wherever possible.

MATERIAL and METHODS

This study was carried out prospectively in the department of Pathology LHMC, New Delhi. Thirty-five symptomatic patients were selected for the present study. These patients had one or more of the following features; growing peripheral lesion on chest ray, positive sputum cytology, and clinical symptom refractory to medication or visible endobronchial mass.

Detailed clinical history, physical examination, hemogram, chest X-ray and bronchoscopy was performed on all 35 cases.

USG guided transthoracic fine needle aspiration cytology (FNAC) was done for peripherally situated lesions.

Bronchoscopy was performed through the transnasal approach, using an Olympus BF- 2TR fibreoptic bronchoscope.

Bronchial brushing (BB) was performed using straight brushes. After the sampling brush was smeared on 5-6 clean slides, these were fixed in 95% ethyl alcohol for PAP, H&E and PAS staining and absolute methanol for Giemsa staining. Bronchial washings were collected after brushing samples. Smears were prepared using sediments and stained by Pap, H&E, Giemsa and Ziehl Neelsen stain. The remaining material was used for cell block preparation wherever possible.

Endobronchial biopsy was performed using a flexible long biopsy forceps and tissue bits were fixed in 10% formalin and processed for histopathological examination.

OBSERVATION

The study group consisted of 35 cases selected on the basis of clinical, radiological and bronchoscopic findings. The age of the patients varied from 18 years to 88 years, and the M:F ratio was 3.3:1. Twenty-five cases (71.4%) were smokers and 10 were non smokers with a smokers to non-smokers ratio of 2.5:1.

Carcinoma was diagnosed in 21 (60%) out of total 35 cases on bronchial biopsy and the remaining 14 cases (40%) showed inflammatory, tuberculous or no significant pathology (Table I).

Bronchial washing showed 10 true positive (TP), 10 true negative (TN), 4 false positive (FP) and 11 false negative (FN) cases whereas bronchial brushing showed 17 TP, 12 TN, 2 FP and 4 FN cases as confirmed on biopsy (Table II).

Bronchial brushing showed good sensitivity (80.9%) and specificity (85.7%) compared to bronchial washing which had sensitivity of 47.6% and specificity of 71.4%. Similarly, the positive predictive value (PPV), negative predictive value (NPV), false negative index (FNI) and false positive index (FPI) of BB were better in brush samples than washings. The accuracy of BB was 82.8 while that of washing was 57.1 (Table III).

Six (60%) of the 10 carcinomas diagnosed by washing were morphologically classified as poorly differentiated

Table I: Diagnosis and distribution of various lesions as confirmed on bronchial biopsy

Diagnosis on bronchial biopsy (n = 35)	
Carcinoma	21 (SCC=18, Adenocarcinoma=1, Small cell carcinoma=2)
Chronic bronchitis	3
Lung abscess	1
Tuberculosis	5
No significant pathology	5

Table II: Test results in tabulated form

Sample	**Test result**				
	TP	**TN**	**FP**	**FN**	**Total**
Bronchial washing	10	10	04	11	35
Bronchial brushing	17	12	02	04	35

Table III: Comparison of indices of bronchial washings and brush cytology

	WASHING *	BRUSHING #
Sensitivity	47.6	80.9
Specificity	71.4	85.7
PPV	71.4	89.4
NPV	47.6	**75**
FNI	52.3	19.0
FPI	28.5	14.2
Accuracy	57.1	82.8

*The 95% confidence interval of sensitivity, specificity, negative and positive predictive value is 0.1089, 0.1207, 0.1207, and 0.1089 respectively.

#The 95% confidence interval of sensitivity, specificity, negative and positive predictive value is 0.085, 0.093, 0.070, and 0.1082 respectively.

carcinoma whereas only 8 (47%) out of 17 carcinomas detected by BB were morphologically classified as poorly differentiated carcinoma. On biopsy, 7 (33%) out of a total of 21 cases were labelled as poorly differentiated carcinoma. Thus morphologic preservation was better in brushing specimens compared to washings.

DISCUSSION

Bronchoscopy and guided techniques have a definitive role in the diagnosis of endobronchial lesions and a combination of washings and brushings with forceps biopsy have shown to increase the sensitivity from 83.17 to 85.64% and 90.65% respectively (1).

Three cases (8.5%) of chronic bronchitis showed chronic inflammatory infiltrate and an increase in number of goblet cells on bronchial brushings. Findings on washings were nonspecific whereas bronchial biopsy showed an increase in the number of goblet cells in the lining epithelium, squamous metaplasia and chronic inflammatory cells in the bronchial wall. Similar features were observed on brushing samples carried out on 200 patients with chronic respiratory symptoms (5).

A single case of lung abscess (2.8%) showed numerous intact and degenerated neutrophils in the necrotic background on brushing and washing. Cell block prepared in this case showed a large amount of necrotic material, bits of lung tissue with intact and degenerated neutrophils. Shroff CP et al. and Tuladhar A et al. found 1.5% and 13.3% cases respectively in their series showing features suggestive of an abscess cavity (5,6).

Five cases (14.2%) were of acid-fast bacillus positive tuberculosis. Bronchial brushings identified only one and in the rest showed chronic inflammatory exudate or granulomatous inflammation. However 3 out of 5 cases were identified by washing. Wallace et al. studied proven cases of tuberculosis and found bronchoscopic specimens to be mostly have a non-specific chronic inflammatory reaction (7). In study by Altaf Bach A et al., bronchial washings smear was positive for acid fast bacilli in 35% of the cases while caseating granulomas were observed in 16.7% and were the only diagnostic feature in 13.3% (8). Daneks, and Bower's and Purohit et al. demonstrated acid fast bacilli in 34% and 42% cases respectively whereas in a study by Kulpati et al. 40% the cases were positive while caseating granulomas were observed in four cases (20%) and were the only diagnostic feature in 15% of the patients (9-11).

Out of a total of 35 cases, carcinoma accounted for 21 (60%). Squamous cell carcinoma was the most common malignancy constituting 18 cases (85.7%), followed by small cell carcinoma with 2 cases (9.5%) and adenocarcinoma in 1 case (4.7%) as confirmed by histological examination.

In study by Rawat J et al. on 107 cases, squamous cell carcinoma accounted for 55 cases (51.4%), adenocarcinoma 12 cases (11.21%), large cell carcinoma 4 cases (3.73%), unclassified 17 cases (15.88%) and small cell carcinoma 19 cases (17.75%) (4).

In the present study, bronchial brushing identified 17 carcinomas including a case of adenocarcinoma and one case of small cell carcinoma whereas only 10 carcinomas were identified by washing that includes a case of adenocarcinoma.

Comparison of the cytological characters of bronchial brushings (Figure 1) and washings (Figure 2) showed that cellularity of the smear was greater in brush specimens with numerous columnar cells noted against a clear background whereas bronchial washing samples tended to shed mostly single malignant cells with occasional cell clusters which were larger in brush than in washing samples.

Bronchial brushing (Figure 3) showed better cellular preservation, nuclear characteristics, chromatin details and nucleoli compared to washing specimens (Figure 4).

Accuracy was highest in the squamous cell type which was in general agreement with the results of studies conducted by Bedrossian et al. (12). However, Tuladar A et al.found that BB was the most sensitive technique for diagnosis of small cell carcinoma (80%) followed by squamous cell carcinoma (35.7%) (6).

Small cell carcinoma tumor cells showed slight variation in size and shape, high nuclear/cytoplasmic ratio, frequent

molding, salt and pepper chromatin and crush artefact. Sturgis CD et al. identified nuclear molding and salt and pepper chromatin as important features for distinguishing small cell carcinoma from non- small cell carcinoma (13).

Statistical evaluation in the present 35 cases of bronchopulmonary lesions was carried out to explore the justification of using a cytologic examination as definitive basis upon which to subject the patient to chemotherapy and radiotherapy without histopathological confirmation of the diagnosis.

Bronchial brush cytology was found to have high sensitivity (80.9%), specificity (85.7%), PPV (89.4%), NPV(75%) and accuracy (82.8%) indicating that there were more chances of bronchial brush cytologic diagnosis to be correct than that of washings. Similar observations were made by Gaur DS et al. who mentioned sensitivity, specificity, PPV, NPV and accuracy of brushing to be 87.3%, 97.6%, 95.4%, 93.10% and 93.90% respectively (3). Rawat J et al. reported sensitivity of endobronchial brushing to be 69.15% and that of washing to be 47.66% (4).

We attempted to confirm with these findings the concept that pulmonary cytology has improved to the point that its sensitivity is high enough to justify its use as a definitive diagnostic tool in those cases where tissue diagnosis is not possible.

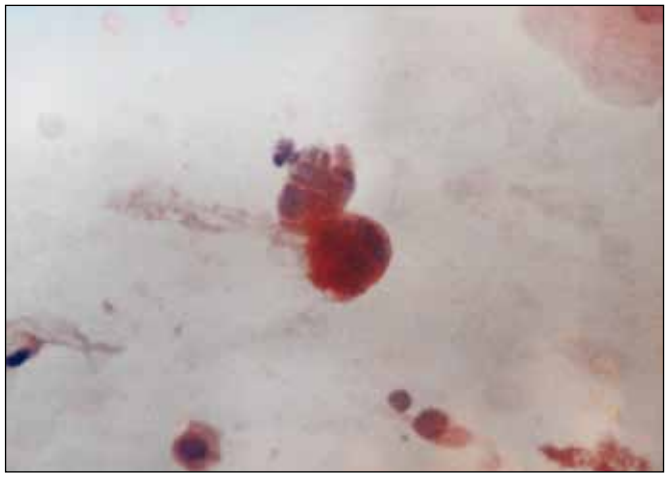

Figure 1: Bronchial brush cytology smear from case of moderately differentiated squamous cell carcinoma shows good cellularity, and better preservation of cellular details (PAP, x100).

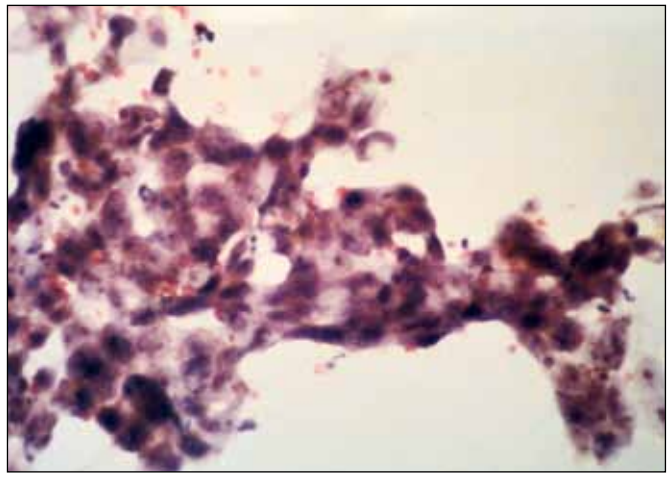

Figure 2: Bronchial washing smear from same case as in figure 1 shows scant cellularity and poorly preserved cellular details (PAP, x100).

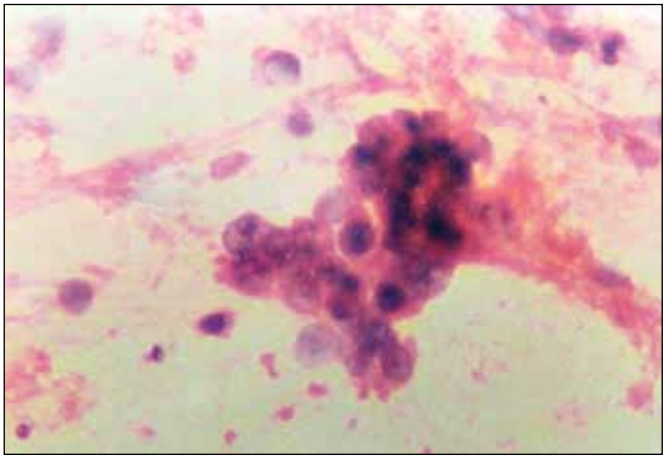

Figure 3: Bronchial brush cytology smear from case of poorly differentiated squamous cell carcinoma shows cluster of cells with crisp nuclear details, coarse chromatin and prominent nucleoli (PAP, x400).

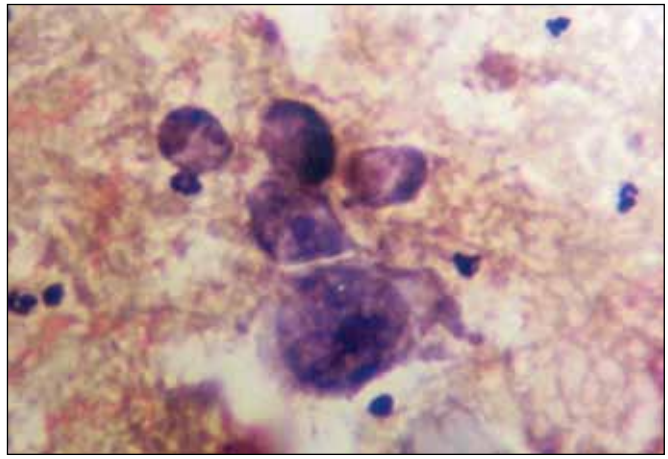

Figure 4: Bronchial washing smear from same case as in figure 3 shows ill defined cellular details (PAP, x400).

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The role of transbronchial needle aspiration in the diagnosis of peripheral lung masses or nodules

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The role of transbronchial needle aspiration in the diagnosis of peripheral lung masses or nodules. K. Katis, E. Inglesos, E. Zachariadis, P. Palamidas, I. Paraskevopoulos, G. Sideris, E. Tamvakopoulou, F. Apostolopoulou, A. Rasidakis. ©ERS Journals Ltd 1995.

ABSTRACT: The purpose of this study was to evaluate the role of transbronchial needle aspiration (TBNA) in the diagnosis of peripheral lung lesions.

We attempted to perform TBNA in 37 patients referred to our hospital for diagnostic evaluation of radiographically evident peripheral masses (23 cases) or nodules (14 cases). None of them had bronchoscopic evidence of endobronchial lesion. The aspirations were performed under fluoroscopic guidance, through a fibreoptic bronchoscope, employing a 21-gauge, 1.3 cm aspirating needle. They were preceded by bronchial brushing and followed by transbronchial biopsy (TBB) of the peripheral lesion. In two cases, the apical nodules were not accessible by any of these procedures. Bronchial washings were also collected immediately after each procedure (brush, TBNA and TBB).

TBNA was diagnostic in 23 of 37 patients (62%) rendering the TBNA yield considerably higher than washing (24%), brushing (27%) or TBB (38%). The addition of TBNA to the combination of TBB, brushing and washing, significantly increased the yield of fibreoptic bronchoscopy in our series from 46% to 70%. No significant complications, such as pneumothorax or major bleeding, occurred either with TBNA or TBB.

In conclusion, our findings suggest that transbronchial needle aspiration is a safe procedure, that can improve the diagnostic yield of bronchoscopy in the diagnosis of peripheral lung masses or nodules.
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Lung tumours often present as peripheral masses or nodules situated beyond the range of even new-generation fibreoptic bronchoscopes. The low diagnostic yield of the standard combination of wash, brush and transbronchial biopsy (TBB) in these abnormalities often requires the use of higher risk procedures, such as percutaneous needle biopsy [1]. In order to improve the yield of bronchoscopy for diagnosis of peripheral masses, the transbronchial needle aspiration (TBNA) technique is being employed in several centres [2–4]. TBNA has been shown to be useful in the diagnosis of primary pulmonary lesions [4–8], in addition to its use as a staging procedure in patients with lung cancer and mediastinal adenopathy [6, 8–13].

In this study, we evaluated the diagnostic yield and the complication rate of TBNA in the diagnosis of lung tumours presenting as peripheral lesions. We also compared TBNA with the standard procedures of wash, brush and TBB in the same group of patients.

Material and methods

Thirty seven consecutive patients (33 males and 4 females) referred to the 2nd Department of Pulmonary Medicine, Sismanogleion Hospital, between January 1991 and September 1992 with undiagnosed peripheral pulmonary lesions on chest radiograph, were included in this prospective study. The age range was 44–78 yrs. Thirty one of the 33 male and one of the four female patients were smokers. During the study period a total of 942 patients underwent bronchoscopy in this department for several reasons. Twenty three patients had pulmonary masses (greater than 3 cm in diameter) whilst 14 patients had nodules (less than 3 cm). We have not included any cases with concomitant endobronchial lesion, nor cases already diagnosed by other means (sputum cytology, sputum microbiology, *etc*). All patients in our series had at least two negative sputum cytological examinations prior to bronchoscopy.

The aspirating needle apparatus employed (Olympus NA-1C) consists of a needle (21-gauge, 1.3 cm length) attached to an inner Teflon catheter housed in a flexible metal sheath into which the needle can be retracted. A 20 ml syringe attached to the proximal end of the inner catheter was used in order to apply suction.

Following premedication, a flexible bronchoscope was introduced transnasally. Provided no endobronchial lesions were identified, the peripheral lesion was approached

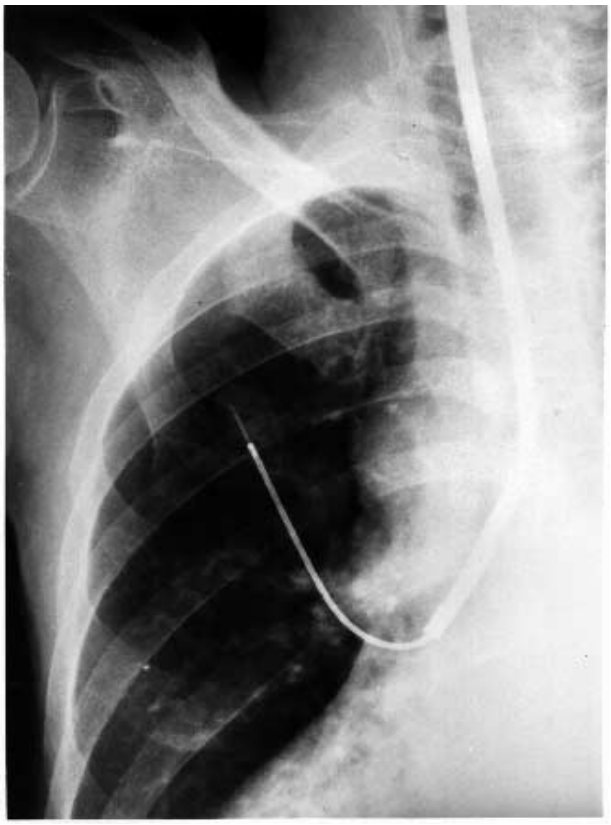

Fig. 1. – Needle aspiration of a peripheral lymph node (2 cm in diameter) situated in the right upper node.

first by brush and then by TBNA and TBB. All procedures were carried out under fluoroscopic guidance by the same team of two endoscopists. The localization of the needle, brush and biopsy forceps was controlled by moving the patient in different positions. Between two and four passes were performed at each lesion with TBNA, and an equal number with brush as well as with biopsy forceps. Bronchial washings were collected immediately after each procedure (brush, TBNA and TBB) by administering and aspirating normal saline *via* the corresponding segmental bronchus.

To perform TBNA, the bronchoscope was inserted into the selected bronchial branch, the needle apparatus was passed through the biopsy channel and advanced under fluoroscopic guidance, until it reached the periphery of the target. The needle was subsequently passed to the lesion and negative suction was applied with the syringe, whilst moving the needle back and forth within the lesion (fig. 1). The needle was then removed and the specimens thus obtained were smeared on glass slides, immersed in 95% alcohol, and sent for cytological processing (Papanicolaou method). The overall duration of the bronchoscopy was less than 25 min in all cases. All patients had a chest radiograph taken 3–4 h after bronchoscopy.

Cytological specimens found to be suspicious for malignancy were considered negative in the data analysis. We compared the proportions of positive results using the χ^2 test.

Table 1. – Yield of TBNA, wash, brush and TBB (n=37)

Procedure	Positive cases	%
TBNA	23	62
Wash	9	24
Brush	10	27
TBB	14	38
TBB + brush + wash	17	46
TBNA + brush + wash	25	68
TBNA + TBB + brush + wash	26	70

TBNA: Transbronchial needle aspiration; TBB: transbronchial biopsy. χ^2 test: TBNA *vs* wash, $p<0.005$; TBNA *vs* brush, $p<0.005$; TBNA *vs* TBB, $p<0.05$; TBB + brush + wash *vs* TBNA + TBB + brush + wash, $p<0.05$.

Results

We attempted to perform TBNA in 37 consecutive patients with radiographically evident peripheral lesions, ranging 1.8–7 cm in diameter. Twenty three patients had masses, *i.e* exceeding 3 cm in size (mean±SD: 5.2±1.2 cm) whereas 14 had nodules, *i.e* less than 3 cm (2.6±0.5 cm). Two patients from the latter group had lesions smaller than 2 cm (1.8 and 1.9 cm). In two other cases, the nodules (2.5 and 2.8 cm), located in the apical segment of the right upper lobe, were inaccessible due to the fact that the brush, biopsy forceps and needle could not be inserted through the apical segmental bronchus.

In 36 patients, a diagnosis of malignancy was finally established (34 bronchogenic and two metastatic carcinomas), whilst one patient had aspergillosis. Diagnosis was obtained by bronchoscopy in 26 patients (the one case of aspergillosis included), by percutaneous needle biopsy in eight patients, and by thoracotomy in three patients. The 26 (70%) patients diagnosed by bronchoscopic procedures included 19 of 23 (83%) with masses and 7 of 14 (50%) with nodules; the difference being nonsignificant ($p>0.5$). TBNA provided diagnostic specimens in 16 out of 23 (69%) patients with masses and 7 out of 14 (50%) patients with nodules; the difference being similarly nonsignificant ($p>0.5$). Thirteen lesions were located in the right upper lobe, nine in the right lower lobe, nine in the left upper lobe and six in the left lower lobe. Diagnosis was established by bronchoscopy in 13 of 22 (55%) upper lobe lesions and 13 of 15 (87%) lower lobe lesions; the difference being nonsignificant ($p>0.5$). The 25 cases of malignancy diagnosed by bronchoscopic procedures included 16 cases in stage I and II, five cases in stage IIIa, three cases in stage IIIb, and one case of small-cell carcinoma in stage II. Epidermoid carcinoma was bronchoscopically diagnosed in 11 patients, adenocarcinoma in six, undifferentiated non-small-cell in five, large-cell in two, and small-cell carcinoma in one patient. There was no difference in cell type between specimens obtained by TBNA, TBB, brush and wash.

The results are summarized in table 1. Cytological examination of TBNA was positive for malignancy in 62% as opposed to 24% for wash ($p<0.005$), 27% for brush ($p<0.005$), and 38% for transbronchial forceps biopsy

($p<0.05$). In nine (24%) patients, TBNA was the only procedure that provided a diagnosis.

The combined yield of TBB, brush and wash was 46%, while the yield of TBNA, brush and wash amounted to 67%. The addition of TBNA to the combination of TBB, brush and wash significantly increased the yield to 70% ($p<0.05$). There were no cases with a negative TBNA and a positive TBB, except for one case of aspergillosis diagnosed by transbronchial biopsy.

No significant complications, such as pneumothorax or major bleeding, occurred in our series with either TBNA or TBB. Insignificant bleeding episodes (less than 10 ml) associated with TBNA stopped without treatment.

Discussion

Transbronchial needle aspiration was first performed by Schieppati in 1958 [8] using a rigid bronchoscope to aspirate mediastinal nodes. Since then, numerous studies have been published on the contribution of TBNA in the diagnosis and staging of lung cancer [14–16]. In 1983, SHURE and FEDULLO [2] were the first to report on the use of a 20-gauge, 1 cm needle for diagnosis of cancer in peripheral masses, and concluded that the yield of bronchoscopy can be considerably increased (69% *versus* 48%) if TBNA is added to the standard combination of TBB, brush and wash.

In 1984, WANG *et al*. [3], having performed TBNA in peripheral lesions with a 22-gauge, 1.3 cm needle, reported a 48% yield, considerably higher than TBB, brush or their combination. When confined to malignant peripheral lesions only, the sensitivity of TBNA was over 69%. SCHENK *et al*. [4] in 1987 reported a 40% yield for TBNA in patients with peripheral lesions. Our study using a 21-gauge, 1.3 cm needle confirmed the utility of TBNA in the diagnosis of peripheral lung masses or nodules. The diagnostic yield of TBNA was 62%, higher than for the other techniques. The addition of TBNA to the standard combination of TBB, brush and wash significantly increased the yield of bronchoscopy in our series from 46 to 70% ($p<0.05$).

Diagnostic yield of TBNA is determined mainly by the accessibility (size, relationship between the airway and the lesion) and the nature of the abnormality. It is obvious that if the bronchoscopist cannot reach the lesion, no diagnosis can be established. In two cases with right apical nodules, it was impossible for the brush, needle and biopsy forceps to enter the apical segmental bronchus; therefore, those lesions were not accessible for needle aspiration, brushing or TBB. As far as the size of the abnormality is concerned, the yield of TBNA is lower for lesions less than 2 cm in diameter compared with those greater than 2 cm [3]. It has also been reported that the yield of TBNA in lesions 2 cm or greater is 50% higher than TBB [2]. Only two of our patients had lesions less than 2 cm in diameter, and in both cases specimens obtained by all procedures were nondiagnostic. The overall yield of TBNA, TBB, brush and wash in our series was not significantly affected by the size of the lesion (83% in masses *versus* 50% in nodules; $p>0.5$). The difference was similarly nonsignificant for TBNA alone (69% in masses *versus* 50% in nodules; $p>0.5$).

The relationship between the airway and the lesion is similarly of great importance [17]. In cases where, due to extrinsic compression either by the lesion itself or by lymphadenopathy, the airway is displaced or obstructed, conventional sampling techniques with brush or TBB cannot obtain diagnostic specimens. In such cases, TBNA can provide invaluable advantages owing to the fact that the needle can pierce the bronchial wall and, thus, reach the lesion. SHURE and FEDULLO [2] reported that in 10 patients with lesions of this type, TBB, brush and wash were negative in all cases, whereas TBNA was positive in eight cases (80%).

Yield is also affected by the nature of the abnormality. WANG *et al*. [3], in a series of 20 patients had three cases with benign nodules (all aspergillosis), none of which was diagnosed by TBNA or any other bronchoscopic procedure. In our single patient with a benign lesion (also aspergillosis) diagnostic information was supplied by TBB; transbronchial needle aspiration was merely "negative for malignancy", failing to determine the nature of the lesion. It should be pointed out that although we have not excluded cases with suspected benign lesions, a great many patients in our series were referred to us from other hospitals or doctors for suspected malignancy after initial clinical and laboratory evaluation. Moreover, most of them were smokers (32 out of 37) belonging to the high risk age group. This might account for the scarcity of benign lesions in this study.

The lack of serious complications, such as pneumothorax or major bleeding, in our series corresponds to the worldwide experience on TBNA of peripheral lesions [2–4] and mediastinal nodes [4–6, 8–13]. The safety of the procedure relates to the small size of the needle, the small size of peripheral pulmonary vessels and the avoidance of pleural surface [3]. Selective bronchoalveolar lavage, whilst it seems to have a rather high yield, often fails to demonstrate the correct cell type [18]. Percutaneous needle biopsy, the main alternative procedure for diagnosis of peripheral lesions, appears to have a higher yield (75–90% in centres with a high degree of experience) but it is associated with a considerable complication rate [19–21]. Pneumothorax, the most common complication, is reported to occur in 20–30% of patients. In our series, the yield of bronchoscopy with the addition of TBNA exceeded 70%, whilst virtually no complications occurred, our findings confirming those from earlier studies.

We conclude that transbronchial needle aspiration is a safe procedure that can improve the diagnostic yield of fibreoptic bronchoscopy in the diagnosis of lung cancer presenting as a peripheral mass or nodule.

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CHEST

Original Research

PULMONARY PROCEDURES

Meta-analysis of Guided Bronchoscopy for the Evaluation of the Pulmonary Nodule

Jessica S. Wang Memoli, MD; Paul J. Nietert, PhD; and Gerard A. Silvestri, MD, FCCP

Background: **The detection of pulmonary nodules (PNs) is likely to increase, especially with the release of the National Lung Screen Trials. When tissue diagnosis is desired, transthoracic needle aspiration (TTNA) is recommended. Several guided-bronchoscopy technologies have been developed to improve the yield of transbronchial biopsy for PN diagnosis: electromagnetic navigation bronchoscopy (ENB), virtual bronchoscopy (VB), radial endobronchial ultrasound (R-EBUS), ultrathin bronchoscope, and guide sheath. We undertook this meta-analysis to determine the overall diagnostic yield of guided bronchoscopy using one or a combination of the modalities described here.**

Methods: **We performed a MEDLINE search using "bronchoscopy" and "solitary pulmonary nodule." Studies evaluating the diagnostic yield of ENB, VB, R-EBUS, ultrathin bronchoscope, and/or guide sheath for peripheral nodules were included. The overall diagnostic yield and yield based on size were extracted. Adverse events, if reported, were recorded. Meta-analysis techniques incorporating inverse variance weighting and a random-effects meta-analysis approach were used.**

Results: **A total of 3,052 lesions from 39 studies were included. The pooled diagnostic yield was 70%, which is higher than the yield for traditional transbronchial biopsy. The yield increased as the lesion size increased. The pneumothorax rate was 1.5%, which is significantly smaller than that reported for TTNA.**

Conclusion: **This meta-analysis shows that the diagnostic yield of guided bronchoscopic techniques is better than that of traditional transbronchial biopsy. Although the yield remains lower than that of TTNA, the procedural risk is lower. Guided bronchoscopy may be an alternative or be complementary to TTNA for tissue sampling of PN, but further study is needed to determine its role in the evaluation of peripheral pulmonary lesions.** ***CHEST 2012; 142(2):385–393***

Abbreviations: ENB = electromagnetic navigation bronchoscopy; NLST = National Lung Screening Trial; PN = pulmonary nodule; R-EBUS = radial endobronchial ultrasound; TTNA = transthoracic needle aspiration; VB = virtual bronchoscopy

The pulmonary nodule (PN) is becoming an increasingly common radiographic finding among patients in the United States. Nearly 45 million CT scan examinations are performed each year, and 11% to 30% (4.5-14 million) of those include an examination of the chest.[1] In the recently released National Cancer Institute-sponsored National Lung Screening Trial (NLST), > 25% of the group who underwent low-dose CT scans of the chest had examinations that were suspicious for lung cancer.[2] With the findings of the NLST indicating a reduction in lung-cancer-specific mortality with CT scanning in at-risk people, the number of patients diagnosed with a PN could increase substantially if screening for lung cancer is broadly

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For related article see page 377

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accepted by the medical community. The prevalence of malignancy in studies evaluating patients with noncalcified nodules ranges from 2% to 82%,[3] and health-care providers are often faced with the diagnostic dilemma of how to manage these patients. The goal is to diagnose malignant nodules promptly, to permit timely surgical resection, while avoiding invasive testing or surgery in patients with benign nodules.

Practice guidelines offer recommendations for the diagnosis and management of the PN.[4] The three general management categories based on the patient's probability of malignancy are watchful waiting with serial CT scans, tissue biopsy for pathologic diagnosis, and direct surgical excision. When biopsy is recommended, transthoracic needle aspiration (TTNA) is currently preferred because it has a diagnostic yield of 90%; however, TTNA also has a pneumothorax rate of about 25%, of which at least 15% requires chest tube insertion (overall chest tube rate of 5%).[4,5] Flexible bronchoscopy is another diagnostic option, but the sensitivity of traditional transbronchial biopsy ranges from 14% to 63%, depending on the size and location of the PN.[5,6] Bronchoscopy with guidance has evolved as a viable option "if the operator has expertise in newer guided techniques."[4]

Within the past decade, new techniques have emerged that offer guidance through the tracheobronchial tree during bronchoscopy to help reach and biopsy PN. Electromagnetic navigation bronchoscopy (ENB) and virtual bronchoscopy (VB) are able to create a virtual bronchoscopic image and a pathway to the PN (Fig 1). ENB can give additional real-time directions to the PN, much like a car's global positioning system for driving to a destination. Using an ultrathin bronchoscope combined with radial endobronchial ultrasound (R-EBUS) through a guide sheath allows the practitioner to visualize the sixth- to eighth-generation bronchi (whereas a traditional bronchoscope can only reach the fourth-generation bronchi), verify that the lesion has been reached, and maintain the position in the periphery for biopsy.

A number of studies have been published using a variety of these technologies to guide the bronchoscopist to the nodule for biopsy. Most have been small, single-institution case series that reported the diagnostic accuracy of the new technology being investigated. We undertook this meta-analysis to assess the overall diagnostic yield and adverse event rate of these technologies in studies that evaluated any one or a combination of these guidance mechanisms for the tissue biopsy of peripheral lung lesions and to compare and contrast these findings with the reported diagnostic yields of traditional bronchoscopy and TTNA.

Materials and Methods

Data Sources

An Ovid MEDLINE (1950 through October 2010) and PubMed database search was performed using "bronchoscopy" and "pulmonary nodule" as terms to identify studies. The search was limited to human subjects. Although the search was not limited to English language studies, no non-English language studies met the inclusion criteria. The reference lists of included studies and review articles were searched manually for other relevant studies.

Study Selection

Review articles and commentaries were excluded from the meta-analysis, but the manuscript and the reference lists of relevant review articles were examined to find other studies. Both prospective and retrospective studies were evaluated for inclusion. The remaining studies were reviewed for relevance. All studies that reported the use of any of the following technologies to evaluate PN were considered for inclusion: ENB or superDimension, VB, endobronchial ultrasound (specifically R-EBUS), ultrathin bronchoscope, and guide sheath. All included studies documented the diagnostic yield of guided bronchoscopy using one or more of the methods described here. Case reports and studies with fewer than five patients were excluded. Studies were excluded if the linear endobronchial ultrasound was used instead of R-EBUS or if guidance was performed with CT scan-fluoroscopy alone. Studies that were performed on inanimate models or on patients without radiographic evidence of nodules to evaluate feasibility were excluded.

Data Synthesis

The articles were reviewed by two investigators (J. W. M. and G. S.). Many of the studies were pilot or feasibility studies undertaken to determine the diagnostic yield of a new technology. The primary technology used and the addition of other methods (eg, VB with R-EBUS) were recorded. The number of lesions and the number of diagnoses made were extracted. The overall diagnostic yield was calculated from the extracted data and compared with the reported diagnostic yield. Although the majority of diagnoses were malignant (primary lung or metastatic disease), other benign causes of the PN (eg, TB, sarcoidosis) were also considered diagnostic if found. If reported in the study, the yield by size ($>$20 mm or $\leq$20 mm) was recorded. The type of study (prospective vs retrospective) was recorded. All adverse events of pneumothorax, respiratory failure, and severe hemorrhage were extracted if reported.

Statistical Analysis

The reported diagnostic yield proportions from each study were aggregated via meta-analysis techniques that incorporated an inverse variance weighting technique and allowed us (via the Q statistic) to determine whether there was significant between-study variation (heterogeneity).[7] We also used a random-effects meta-analysis approach that yielded similar findings (results not presented). These processes account for the study sample size and study heterogeneity. Inverse-variance weighted means of the studies' diagnostic yields and their 95% CIs were computed across all studies. Studies that used a specific method of biopsy were grouped (ie, all studies that used VB were grouped even if a combination of technologies was evaluated in an individual study), and the same computations for inverse variance weighted means were performed for each group. Because diagnostic yield for study i is

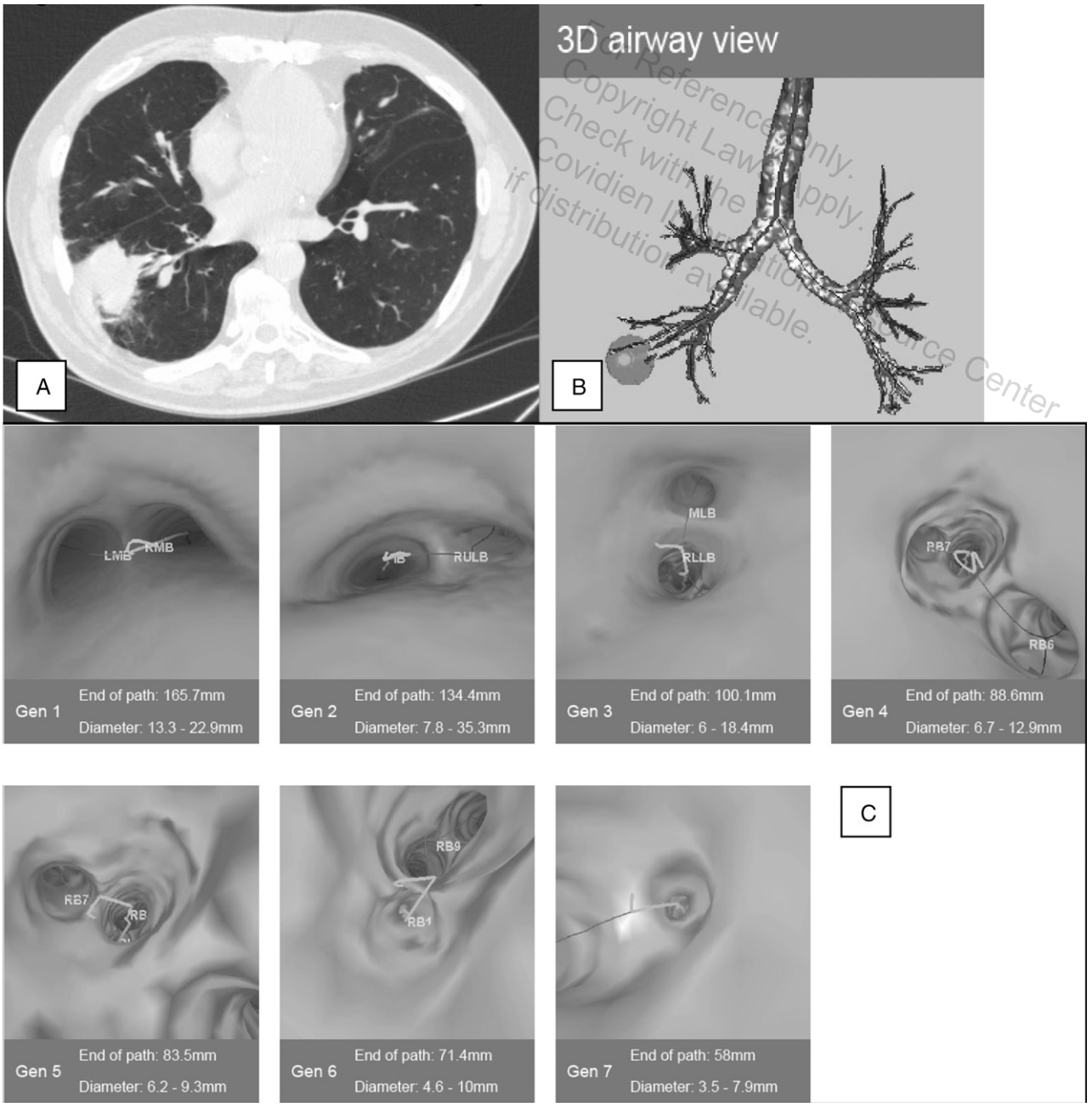

FIGURE 1. A, Chest CT image of a right lower lobe pulmonary lesion in a 78-year-old smoker. B, 3-D reconstruction of the tracheobronchial tree with the nodule outlined. C, Airway reconstruction of the pathway to the peripheral lesion. (Figure created and provided by Broncus Technologies, Inc.) Gen = generation; LMB = left mainstem bronchus; MLB = middle lobe bronchus; RB = right bronchial; RLLB = right lower lobe bronchus; RMB = right mainstem bronchus; RULB = right upper lobe bronchus.

a percentage ($Yield_i$) out of the study sample size (n_i), its variance is simply

$$\sigma_i^2 = \frac{Yield_i \times (1 - Yield_i)}{n_i}$$

using standard binomial theory.[8] The reciprocal of this variance measure

$$w_i = \frac{1}{\sigma_i^2}$$

served as a weight within the calculation of the weighted mean diagnostic yield for this meta-analysis:

$$\text{Inverse variance weighted diagnostic yield} = \frac{\sum_{i=1}^{N} w_i \times Yield_i}{\sum_{i=1}^{N} w_i}$$

where N reflects the total number of eligible studies.

Results

The MEDLINE and PubMed searches identified 140 and 309 potential studies, respectively. A thorough review of the reference lists of related studies uncovered an additional 29 studies. From these, a total of 39 studies met the inclusion criteria and were included in the analysis (Fig 2). The included studies were published between 2002 and October 2010. All studies reported the diagnostic yield of bronchoscopic biopsy of PN using at least one of five guidance techniques: VB, ENB, R-EBUS, guide sheath, or ultrathin bronchoscope. Six of the studies were retrospective. A total of 3,004 patients with 3,052 lesions from the 39 studies were included in this meta-analysis. Table 1[9-47] lists the study characteristics and summarizes the findings for each of the studies (Fig 3).

The inverse variance weighted diagnostic yield was 70.0% with a 95% CI of 67.1% to 72.9% (Table 2). Across the studies, the diagnostic yield ranged from 46.0% to 86.2% (Fig 2), and the Q statistic ($\chi^2_{[30df]} = 119.4$) indicated that there was significant ($P < .0001$) variation in the diagnostic yield estimates. Table 2 lists the pooled diagnostic yield estimates for groups of studies that used various technologies, along with group-specific heterogeneity test results. Diagnostic yield appeared to be highest (73.2% [95% CI, 64.4% to 81.9%]) when a guide sheath was used, although there was significant variation across studies (Q statistic = 63.8, $P < .0001$). The yields for VB (72.0% [95% CI, 65.7% to 78.4%]) and R-EBUS (71.1% [95% CI, 66.5% to 75.7%) were also higher than the overall weighted diagnostic yield.

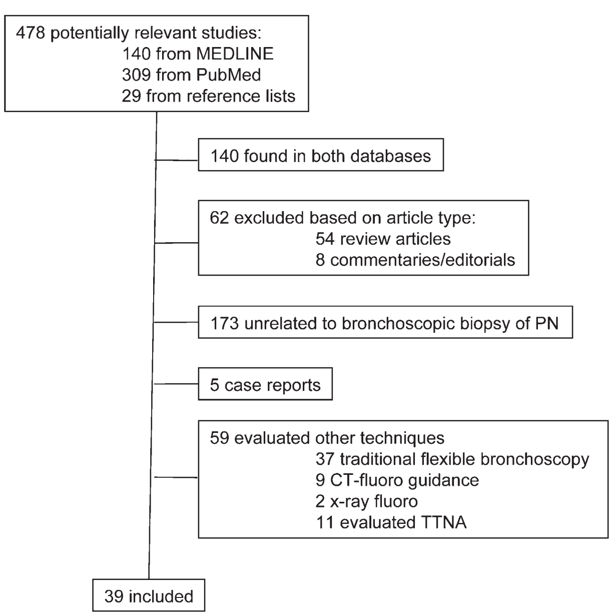

Figure 2. Literature search and selection. fluoro = fluoroscopy; PN = pulmonary nodule; TTNA = transthoracic needle aspiration.

Twenty-two studies evaluated the effect of size on the diagnostic yield (Table 3). Of these, 20 studies reported the diagnostic yields for lesions ≤ 20 mm and > 20 mm (in two studies, 30 mm was used as the size criteria, and those were excluded from this subanalysis). From these, the weighted diagnostic yields of the 629 lesions ≤ 20 mm and the 767 lesions > 20 mm were 60.9% (95% CI, 54.0% to 67.7%) and 82.5% (95% CI, 78.6% to 86.4%), respectively. The weighted difference in diagnostic yield for these two measurement groups is 19.6% (95% CI, 11.7% to 27.6%; $P < .001$).

Of the studies included in the meta-analysis, 28 (2,156 total patients) reported on the rate of adverse events. The overall adverse event rate from those reported is 1.5% (n = 33) with the majority reporting pneumothorax. Thirty-two patients (1.5%) developed a pneumothorax (range 0.0% to 7.5% across studies) and, of these, 14 (0.6%) required placement of a chest tube and one underwent aspiration without placement of a chest tube. One patient (0.1%) developed respiratory failure requiring intubation. No episodes of significant bleeding or death were reported.

Discussion

This study has several important findings that may influence our current practice and approach to the evaluation and management of PN. First, the pooled diagnostic yield of 70% is much higher than yields reported previously using traditional bronchoscopic techniques.[5,6] Second, although the diagnostic yield for guided bronchoscopic techniques is lower than that reported for TTNA, the adverse event rate is also significantly lower. Third, the yield is dependent on the size of the lesion. Finally, the use of VB, R-EBUS, and a guide sheath may have a greater influence on the diagnostic yield of bronchoscopic evaluation of PN.

The current algorithms for management of PN rely heavily on TTNA when a pathologic diagnosis is desired.[4,48] TTNA does have a 90% chance of confirming a diagnosis (range, 76% to 90%), but some report a pneumothorax rate as high as 40%.[4,5,49-57] Additionally, the diagnostic yield is influenced by the size of the lesion, the size of the needle, the number of passes, and the presence of rapid on-site evaluation.[4,5,53-56] The location of the lesion in the lungs, peripheral vs central, may also influence the diagnostic yield of TTNA.

In contrast, the sensitivity of the traditional bronchoscopic biopsy is only 34% for nodules ≤ 2 cm, and has been found to be as low as 14%.[5,6] The sensitivity increases to 63% when nodules are > 2 cm in size, but decreases as the distance from the hilum increases. A lesion having a bronchus sign (the finding of a bronchus leading to the lesion) increases the success of transbronchial biopsy and brushing.[58] Recently, technology

Table 1—*List of Studies and Results Included in Meta-analysis*

No.	Study	Year	Pro/Retro	Technology	No. Lesions	No. Diagnosed	Yield, %	Adverse
1	Herth et al[9]	2002	Pro	R-EBUS	50	40	80	1 PTX (1 CTI)
2	Shirakawa et al[10]	2004	Pro	R-EBUS, GS	51	42	82.4	No report
3	Yang et al[11]	2004	Retro	R-EBUS	122	80	65.6	None
4	Shinagawa et al[12]	2004	Pro	U, VB	26	17	65.4	No report
5	Yamamoto et al[13]	2004	Pro	U	35	21	60	No report
6	Kikuchi et al[14]	2004	Pro	R-EBUS, GS	24	14	58.3	1 PTX (1 CTI)
7	Kurimoto et al[15]	2004	Pro	R-EBUS, GS	150	116	77.3	None
8	Becker et al[16]	2005	Pro	R-EBUS, ENB	29	20	68.9	1 PTX (1 CTI)
9	Hautmann et al[17]	2005	Pro	ENB	5	3	60	None
10	Asahina et al[18]	2005	Pro	U, VB, R-EBUS, GS	30	19	63.3	None
11	Paone et al[19]	2005	Pro	R-EBUS	87	66	75.8	None
12	Herth et al[20]	2006	Pro	R-EBUS, GS	54	38	70.4	1 PTX (1 CTI)
13	Schwarz et al[21]	2006	Pro	ENB	13	9	69.2	None
14	Gildea et al[22]	2006	Pro	ENB	54	40	74.1	2 PTX (2 CTI)
15	Asano et al[23]	2006	Pro	U, VB	38	31	81.6	No report
16	Shinagawa et al[24]	2007	Pro	U, VB	71	50	70.4	No report
17	Shinagawa et al[25]	2007	Pro	U, VB	85	56	65.9	No report
18	Dooms et al[26]	2007	Pro	R-EBUS	50	34	68	None
19	Makris et al[27]	2007	Pro	ENB	40	25	62.5	3 PTX (1 CTI)
20	Eberhardt et al[28]	2007	Pro	R-EBUS, ENB, GS	118	85	72	7 PTX (4 CTI, 1 aspiration)
21	Tachihara et al[29]	2007	Pro	U, VB	96	60	62.5	None
22	Yoshikawa et al[30]	2007	Pro	R-EBUS, GS	123	106	86.2	1 PTX (0 CTI)
23	Eberhardt et al[31]	2007	Pro	ENB	92	62	67.4	2 PTX (0 CTI), 1 intub
24	Yamada et al[32]	2007	Retro	R-EBUS, GS	158	106	67.1	No report
25	Wilson et al[33]	2007	Retro	ENB	279	167	59.9	3 PTX (0 CTI)
26	Asano et al[34]	2008	Pro	U, VB, R-EBUS, GS	32	27	84.4	No report
27	Fielding et al[35]	2008	Pro	R-EBUS, GS	140	93	66.4	2 PTX (0 CTI)
28	Oki et al[36]	2008	Pro	U	98	68	69.4	None
29	Lamprecht et al[37]	2009	Retro	ENB	13	10	76.9	None
30	Huang et al[38]	2009	Retro	R-EBUS	83	44	53	2 PTX (0 CTI)
31	Weiner et al[39]	2009	Pro	VB	50	29	58	No report
32	Eberhardt et al[40]	2009	Pro	R-EBUS, GS	100	46	46	3 PTX (2 CTI)
33	Bertoletti et al[41]	2009	Pro	ENB	53	41	77.3	2 PTX (1 CTI)
34	Chao et al[42]	2009	Pro	R-EBUS	182	126	69.2	No report
35	Oki et al[43]	2009	Pro	U, R-EBUS	71	49	69	None
36	Iwano et al[44]	2011	Retro	VB	122	96	78.7	No report
37	Seijo et al[45]	2010	Pro	ENB	51	34	66.7	None
38	Disayabutr et al[46]	2010	Pro	R-EBUS	152	101	66.4	None
39	Eberhardt et al[47]	2010	Pro	U, VB	25	20	80	1 PTX (0 CTI)

CTI = chest tube insertion; ENB = electromagnetic navigation bronchoscopy; GS = guide sheath; intub = intubation; pro = prospective; PTX = pneumothorax; R-EBUS = radial endobronchial ultrasound; retro = retrospective; U = ultrathin bronchoscope; VB = virtual bronchoscopy.

has advanced to allow for better visualization of more distal airways with ultrathin bronchoscopes and endobronchial ultrasound. Additionally, virtual re-creation of the airway leading to the peripheral lesions, and navigation using improved CT imaging combined with ENB and VB, allows for direction and guidance to those PN. With the advancement of these new modalities, the recommendations for diagnosing a PN allow for the use of bronchoscopy if newer guidance techniques are available.[4] Few data, though, exist to determine if guided bronchoscopy is equivalent to TTNA or if these procedures are complementary, depending on the location of the target lesion and an assessment of patient risk.

This meta-analysis includes >3,000 cases of guided bronchoscopy performed for the diagnosis of PN. It establishes that the weighted diagnostic yield is significantly better than that reported for traditional flexible bronchoscopy, but the yield still remains lower than that of TTNA.[4] Several studies included reported yields that approached the 90% yield of TTNA. Most notably, the study with the highest diagnostic yield using guided bronchoscopy compared a single method to a combination of technologies. Eberhardt et al[28] studied ENB alone, R-EBUS alone, and ENB combined with R-EBUS. The diagnostic yields of ENB, R-EBUS, and the combination of the two were 59%, 69%, and 88%, respectively. Although R-EBUS alone was better than ENB alone, the combination increased the yield to levels comparable to that of TTNA, suggesting that a combination of modalities may improve diagnostic yield.

Our results show wide variation in diagnostic yields among studies, which may be due to the differences

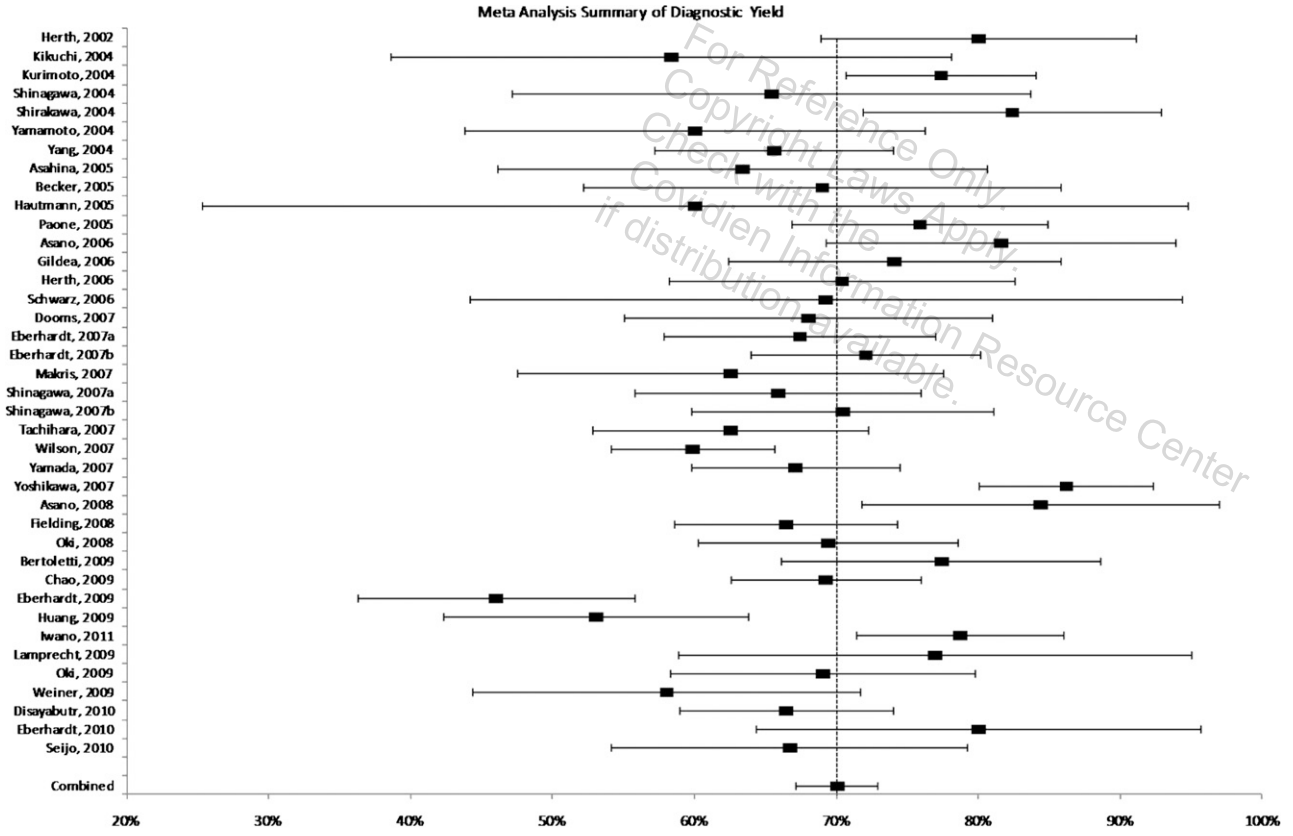

FIGURE 3. Overall summary of the diagnostic yields of the studies included in this meta-analysis.

in the definition of PN; the variability in the location of lesions targeted, which affects biopsy method; and the many options for obtaining a biopsy specimen, which have varying yields and risks. Patient selection was not uniform: Some defined the PN as a well-circumscribed opacity of ≤3 cm surrounded by aerated lung, whereas others defined it as a nodule farther than the fourth- or fifth-generation bronchi. The location of the lesion may also affect the ability to reach the lesion, but the location of the PN is not reported in all studies. Additionally, the various techniques used and operator ability can affect yield.

In this meta-analysis, three modalities had a higher diagnostic yield than the overall yield: VB, R-EBUS, and the use of a guide sheath. With R-EBUS, the location of the bronchoscope at the lesion can be verified with real-time visualization, and the guide sheath acts as an extended working channel to maintain that location during biopsy. Using these two technologies may help ensure that the lesion is definitively reached for biopsy. The finding of a higher weighted diagnostic yield with VB is more interesting, especially because it had a higher yield than ENB (Table 2). ENB has a VB component that is simulated prior to the bronchoscopy. In addition, ENB has real-time navigation that subsequently directs the bronchoscopist to the lesion, potentially making it more accurate. However, the yield of ENB in this meta-analysis was less than that of VB alone. This may have depended on the software that generated the virtual picture, as well as on the operator.

Further subanalysis of the patients included in this meta-analysis supports the previous finding that diagnostic yield increases as the size of the PN increases.[6] Of the studies that reported the diagnostic yield categorized by size, the yield was significantly higher for larger lesions. We are unable to comment on the effect of location on diagnostic yield because so few studies reported the yield in relation to the lobar location of the PN.

Of the studies that included information on adverse events, the rates of pneumothorax, hemorrhage, and

Table 2—*Inverse Weighted Diagnostic Yield Overall and by Modality*

Technology	Studies, No.	Weighted Proportion, %	95% CI	Q Statistic	Q *P* Value
VB	10	72.0	(65.7-78.4)	21.0	.01
ENB	11	67.0	(62.6-71.4)	13.3	.21
GS	10	73.2	(64.4-81.9)	63.8	< .0001
U	11	70.0	(65.0-75.1)	15.2	.12
R-EBUS	20	71.1	(66.5-75.7)	84.2	< .0001
All	39	70.0	(67.1-72.9)	119.4	< .0001

See Table 1 legend for expansion of abbreviations.

Table 3—*Studies That Reported on Diagnostic Yield Based on Size*

No.	Study/Year	Lesions > 20 mm			Lesions ≤ 20 mm		
		Lesions, No.	Diagnoses Made, No.	Yield, %	Lesions, No.	Diagnoses Made, No.	Yield, %
1	Kikuchi et al[14]/2004	9	6	66.7	15	8	53.3
2	Kurimoto et al[15]/2004	69	57	82.6	81	59	72.8
3	Asahina et al[18]/2005	12	11	91.7	18	8	44.4
4	Schwarz et al[21]/2006	11	8	72.7	2	1	50
5	Gildea et al[22]/2006	23	17	73.9	31	23	74.1
6	Asano et al[23]/2006	12	10	83.3	26	21	80.8
7	Dooms et al[26]/2007	39	32	82.1	11	2	18.2
8	Makris et al[27]/2007	20	15	75	20	10	50
9	Eberhardt et al[28]/2007	30	20	66.7	9	7	77.8
10	Tachihara et al[29]/2007	19	18	94.7	77	42	54.5
11	Yoshikawa et al[30]/2007	86	78	90.7	37	28	75.7
12	Eberhardt et al[31]/2007	57	40	70.2	35	22	62.9
13	Yamada et al[32]/2007	84	65	77.4	74	41	55.4
14	Asano et al[34]/2008	17	16	94.1	15	11	73.3
15	Oki et al[36]/2008	75	55	73.3	23	13	56.5
16	Lamprecht et al[37]/2009	9	7	77.8	4	3	75
17	Eberhardt et al[40]/2009	0	0		100	46	46
18	Bertoletti et al[41]/2009	46	37	80.4	7	3	42.9
19	Oki et al[43]/2009	57	44	77.2	14	5	35.7
20	Iwano et al[44]/2011	92	74	80.4	30	22	73.3

respiratory failure were very low. Most of the patients who suffered an adverse event had a pneumothorax, but fewer than one-half of those needed management with a chest tube. One other patient developed respiratory failure requiring intubation and mechanical ventilation. Thus, the adverse event rate that required intervention was only 0.7%. When compared with the 25% pneumothorax rate and an overall 5% chest tube rate with TTNA, the pneumothorax (1.5%) and chest tube (0.6%) rates with guided bronchoscopy were significantly lower.[4]

This meta-analysis does not give clear evidence that guided bronchoscopy is an adequate alternative to TTNA in all cases in which a diagnosis of PN is needed. It does show that using guidance when evaluating a PN will increase the yield of bronchoscopy, as will biopsy of lesions > 20 mm. Because patient selection varies for those referred for TTNA compared with those referred for evaluation by bronchoscopy, the diagnostic yield and the adverse event rate of guided bronchoscopy needs to be prospectively compared with those of TTNA. A multicenter, prospective, randomized control trial would provide a direct comparison between guided bronchoscopy and TTNA, which may allow us to determine the most advantageous use of these guided biopsy modalities. As we continue to understand these new technologies better, including their limitations, we may find that the various options to reach and biopsy PN are complementary; the decision may be based on location (center vs periphery), size, and expertise available. Further study may help to determine the appropriate role of these emerging technologies.

Conclusions

In summary, this meta-analysis, based on 39 studies with > 3,000 patients spanning the past decade, shows that guided bronchoscopy for evaluation of PN provides a reasonably high diagnostic yield with a low side-effect profile. The release of the NLST findings and the continued interest in radiographic lung cancer screening will likely lead to an increase in the number of PN identified. As the current modalities evolve and new technologies are developed, the capability of bronchoscopy to reach peripheral PN for diagnostic and treatment purposes will continue to improve. It has become increasingly important to determine the role of these guided procedures in the evaluation of patients, with the goal of these emerging techniques to be to identify malignancy quickly while limiting risk to the patient.

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Dr Silvestri: contributed to the study concept and design, analysis and interpretation of the data, and drafting of the manuscript.
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Index terms:
Biopsies, complications, 60.126, 60.4129, 60.458
Lung, biopsy, 60.126

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Abbreviations:
FNAB = fine-needle aspiration biopsy
TTNB = transthoracic needle biopsy

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Transthoracic Needle Biopsy of the Lung: Results of Early Discharge in 506 Outpatients[1]

PURPOSE: To determine the safety of early discharge (30 minutes) after transthoracic needle biopsy (TTNB) of the lung.

MATERIALS AND METHODS: In a prospective study of 506 consecutive outpatients who underwent TTNB of the lung, 440 patients underwent fine-needle aspiration biopsy (FNAB) only, and 66 underwent FNAB and core biopsy. Patients were discharged after 30-minute postbiopsy chest radiography if there was no pneumothorax. Patients were discharged after 60-minute chest radiography if they had a stable asymptomatic pneumothorax. These patients were followed up 1 day and/or 1 week after biopsy to identify delayed complications. Patients with a symptomatic or enlarging pneumothorax were treated with an 8-F pigtail catheter attached to a Heimlich valve, discharged, and followed up 24 hours later for chest tube removal.

RESULTS: The pneumothorax rate was 22.9% (116 patients). Eighty-one patients (16.0%) had an asymptomatic pneumothorax, and 33 (6.5%) had a pigtail catheter in place. Seven (1.4%) patients developed a symptomatic pneumothorax after discharge; two of them (0.4%) underwent large-bore chest tube insertion. The other five (1.0%) underwent delayed pigtail catheter insertion. There were no deaths or other major complications.

CONCLUSION: Early discharge after outpatient TTNB of the lung is associated with little morbidity and no mortality.

Transthoracic needle biopsy (TTNB) of pulmonary lesions is traditionally performed as an outpatient procedure. It is safe, accurate, sensitive, and can obviate surgical diagnosis. The most common major complication is pneumothorax. The incidence of pneumothorax reported in the literature during the past 30 years (1–12) is 5%–57%, with a 1.6%–17.0% chest tube insertion rate.

In spite of the frequent complication of pneumothorax, there is no uniform method of surveillance for its detection after TTNB. It has been estimated that most pneumothoraces occur within 30 minutes after biopsy (13). In a retrospective study of 673 TTNB procedures, Perlmutt et al (11) tried to determine the optimum time for performing postbiopsy chest radiography. Of the pneumothoraces requiring chest tube insertion, 88% were detected immediately, and none requiring intervention were detected after 1-hour radiography. A 30-minute radiograph was not obtained. Despite their conclusions, the authors recommended obtaining 1- and 4-hour postbiopsy radiographs in all outpatients, even if there was no pneumothorax on the 1-hour radiographs.

Even as recently as 1998, Moore (14) recommended 1-, 2-, and 3-hour chest radiography as routine surveillance after biopsy, and some authors (15) admit patients to a surgical day care unit before and after the procedure and incur costs in addition to those of the procedure. To our knowledge, the shortest reported observation period from lung biopsy to discharge of patients without a pneumothorax is 1 hour. Even so, the authors of the study in which this occurred (9) have their patients return to the hospital for 24-hour postprocedure chest radiography.

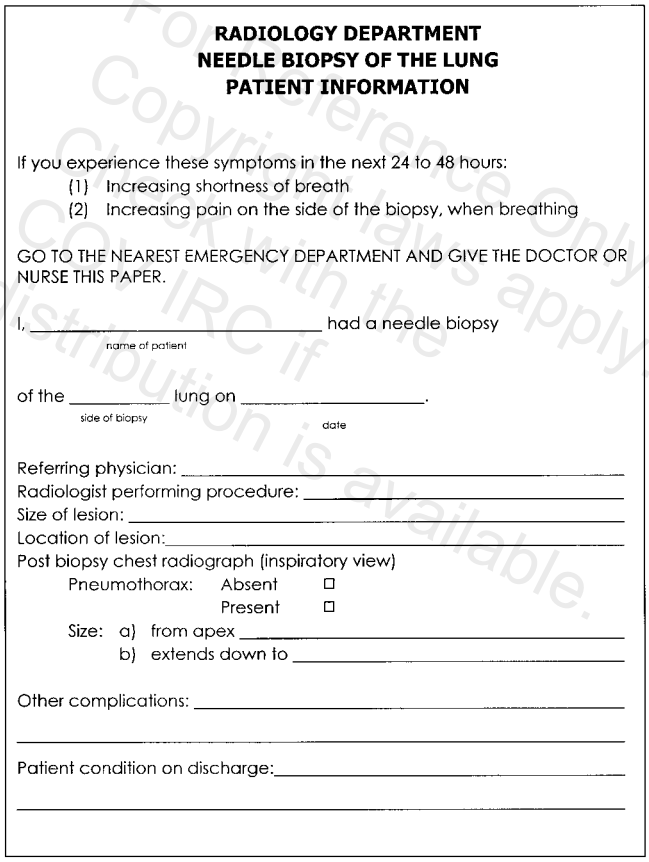
Since 1986, we have performed approximately 4,000 TTNBs. Almost all were performed on a completely outpatient basis with fluoroscopic guidance. Three to six biopsies are routinely performed per day, with patients scheduled 30 minutes apart; the procedure itself lasts 10–15 minutes. Our postbiopsy protocol has consisted of obtaining a chest radiograph 30 minutes after biopsy and discharging the patient if there is no pneumothorax. Although this procedure had never posed a problem to the patients as far as they knew, the purpose of the current study was to prospectively evaluate the safety of early discharge after TTNB of the lung.

MATERIALS AND METHODS

From November 1997 to April 1999, we conducted a prospective study of 506 consecutive outpatient lung biopsies. Our institution's research ethics board determined that its formal review and approval were not required for this study. Four hundred ninety-eight biopsies were performed with fluoroscopic guidance; six, with computed tomographic (CT) guidance; and two, with ultrasonographic guidance. Four hundred forty procedures consisted of fine-needle aspiration biopsy (FNAB) only, whereas 66 consisted of FNAB and core biopsy. After informed consent was obtained from the patients, the procedures were performed by two radiologists on the medical staff (C.J.D., F.R.M.), one fellow, and radiology residents. The biopsies performed by the fellow and residents were all directly supervised by one of the two chest radiologists.

Demographic information collected included patient age and sex, size and location of the lesion, number of pleural punctures, types of needle used, patient smoking history, and presence or absence of emphysema on the chest radiograph or CT scan. A visual assessment method similar to the pathologic panel-grading system was used for grading emphysema in patients who had undergone CT (16). Patients with less than 25% of the pulmonary parenchyma affected by emphysema received a classification of mild; patients with 26%–59%, moderate; and patients with more than 60%, severe.

The only contraindication to biopsy was anticoagulation therapy. Patients also were excluded from the study if no aerated lung was traversed during the biopsy. All complications were recorded, including whether pneumothorax was present or absent, and size if present; whether catheter placement was necessary; and whether patients had hemoptysis or pleuritic chest pain that was unrelated to pneumothorax.



RADIOLOGY DEPARTMENT
NEEDLE BIOPSY OF THE LUNG
PATIENT INFORMATION

If you experience these symptoms in the next 24 to 48 hours:
(1) Increasing shortness of breath
(2) Increasing pain on the side of the biopsy, when breathing

GO TO THE NEAREST EMERGENCY DEPARTMENT AND GIVE THE DOCTOR OR NURSE THIS PAPER.

I, _____ had a needle biopsy
name of patient

of the _____ lung on _____.
side of biopsy date

Referring physician: _____
Radiologist performing procedure: _____
Size of lesion: _____
Location of lesion: _____
Post biopsy chest radiograph (inspiratory view)
Pneumothorax: Absent ☐
Present ☐
Size: a) from apex _____
b) extends down to _____

Other complications: _____

_____

Patient condition on discharge: _____

_____

Figure 1. Information sheet given to every patient after lung biopsy.

After biopsy, all patients were placed in the decubitus position, with the side of the body on which biopsy had been performed facing down. We did not routinely monitor oxygen saturation after biopsy. A posteroanterior inspiratory chest radiograph was obtained with the patient in an erect position 30 minutes after biopsy, and the patient was again placed in the decubitus position, with the biopsy side down. If there was no pneumothorax, the patient was discharged with an information sheet. If there was a small asymptomatic pneumothorax, the patient was left in the decubitus position, with the biopsy side down, for another 30 minutes, and a posteroanterior inspiratory chest radiograph was obtained with the patient sitting erect 60 minutes after biopsy. If there had been no change in the size of the pneumothorax, patients also were discharged with the information sheet. All of the postbiopsy chest radiographs were interpreted by one of the two chest radiologists who performed or supervised the procedure.

Patients were telephoned 24 hours (n = 464) and/or 1 week (n = 506) after biopsy. Patients were asked whether they had experienced delayed symptoms such as shortness of breath or chest pain and whether this had led to repeat chest radiography and/or chest tube insertion at another institution.

The information sheet (Fig 1) instructed patients to return to the nearest emergency department if they developed symptoms after leaving the radiology suite. They were instructed to give the sheet to the emergency medicine physician, since it provided information regarding the side of the body on which biopsy had been performed, as well as the presence or absence of pneumothorax and its size, if present, at discharge. Other complications also were documented on this sheet.

The indication for catheter drainage was symptomatic or enlarging pneumothorax. An 8-F catheter (Navarre; Biomedical, Plymouth, Minn) was inserted through the second anterior intercostal space in the midclavicular line on the

TABLE 1
Summary of Complications in 506 Patients Who Underwent Biopsy

Complication	No. of Patients
Pneumothorax at discharge*	81 (16.0)
Chest tube placement*	35 (6.9)
8 F, immediate	28 (5.5)
8 F, delayed	5 (1.0)
Large bore, immediate	0
Large bore, delayed	2 (0.4)
Tension pneumothorax	0
Admissions	8 (1.6)
Pleuritic chest pain	12 (2.4)
Hemoptysis	35 (6.9)
Vasovagal response	4 (0.8)

Note.—Data in parentheses are percentages.
* The total number of patients with pneumothorax was 116 (22.9%), or the number of patients with pneumothorax at discharge plus the number of patients who underwent chest tube placement.

TABLE 2
Time from Biopsy to Delayed Catheter Insertion

Time	No. of Patients (n = 7)
3 h	2
8 h	1
2 d	2
5 d	1
6 d	1

TABLE 3
Size of Pneumothorax at Discharge

Pneumothorax Size at Discharge (cm from first posterior rib)	No. of Patients
<1.0	11
1.0–1.4	21
1.5–1.9	6
2.0–2.4	22
2.5–2.9	4
3.0–3.9	13
4.0–4.9	3
5.0	1

affected side of the body and attached to a Heimlich valve (Bard-Parker, Franklin Lakes, NJ). A 14-gauge angiocatheter was inserted in the same location prior to chest tube placement only in the case of a tension pneumothorax.

A posteroanterior inspiratory chest radiograph was obtained with the patients sitting erect after catheter placement to ensure complete or nearly complete resolution of the pneumothorax. If complete pleural symphysis was not present and the patient continued to have symptoms, the patient was admitted for underwater suction. If there was satisfactory repeat expansion of the lung, the patient was discharged with the tube in place and returned to our department after 24 hours. The tip of the Heimlich valve was then placed in a cup of water, and the patient was instructed to cough. If there was no bubbling, then the tube was removed, and a chest radiograph was obtained to document resolution of the pneumothorax prior to discharge. If an air leak was present, the tube was left in situ, and the patient returned home and was followed up every 24 hours until the leak had stopped. If subcutaneous emphysema developed 24 hours after catheter placement, a chest radiograph was obtained, since the emphysema was a clue that the air leak was beyond the capacity of the Heimlich valve. If the pneumothorax was larger than that seen on the chest radiograph obtained immediately after catheter placement, then the patient was admitted for underwater suction. If patients developed symptoms of a delayed pneumothorax and returned to our institution, they were referred back to us for 8-F catheter insertion and followed up in the same manner as detailed previously. These cases were labeled as delayed catheter insertions.

The rates of pneumothorax and of immediate and delayed catheter insertion were calculated. The percentage of patients who were admitted or experienced chest pain, hemoptysis, or a vasovagal reaction was also tabulated. The χ^2 test was performed to determine whether there was a significant difference between the rate of pneumothorax and catheter placement in patients who underwent FNAB versus in those who underwent FNAB and core biopsy.

RESULTS

There were 229 women and 277 men (age range, 28–94 years; mean patient age, 66 years; median age, 67 years). The mean lesion diameter was 2.9 cm, with a median of 2.5 cm and a range of 0.4–10.0 cm. One hundred eighty-seven of the lesions on which biopsy was performed were 1.0–2.0 cm, whereas 21 were less than 1.0 cm. A mean of two and a half pleural punctures was performed per patient, with a range of one to four. In 422 patients, we used a 22-gauge spinal needle, whereas in 80 patients, we used a 19-gauge introducer needle through which a 22-gauge Chiba needle or a 20-gauge core biopsy needle was introduced. In four patients, a 17-gauge needle was used as an introducer to an 18-gauge core biopsy gun.

There were 260 smokers. Forty-one patients had quit smoking 1–10 years before the biopsy, and 57 had quit smoking more than 10 years prior to the biopsy. There were 74 nonsmokers. Smoking history was unknown in 74 patients. One hundred ninety-nine patients had no visible emphysema on the chest radiograph or CT scan, 206 had mild emphysema, 85 had moderate emphysema, and 16 had severe emphysema.

Table 1 summarizes the complications in the 506 patients who underwent biopsy. The pneumothorax rate was 22.9% (116 patients). Eighty-one (16.0%) patients were discharged with a small asymptomatic pneumothorax, and 35 (6.9%) underwent chest tube placement. Of these 35, 33 had 8-F tubes inserted by us at our institution. Twenty-eight of these 33 had tubes placed prior to discharge; these procedures were labeled as immediate catheter insertions. The other five had tubes placed by us when the patients returned to the hospital. Three of these five patients were aware of a small asymptomatic pneumothorax after biopsy. These patients' procedures were labeled as delayed catheter insertions.

Results of the χ^2 test showed no difference in the rates of pneumothorax and catheter placement in patients who underwent FNAB only versus those who underwent FNAB and core biopsy ($P > .5$). The rates were 16.6% and 7.0%, respectively, for FNAB and 15.2% and 6.1%, respectively, for core biopsy and FNAB.

Only two patients underwent large-bore (28-F) tube insertion by a surgeon at a peripheral hospital. These procedures were both delayed chest tube insertions. One patient was aware of the presence of a small pneumothorax after biopsy.

Twelve (2.4%) patients experienced pleuritic chest pain that was unrelated to a pneumothorax. These patients were given analgesics, observed until the pain resolved, and then discharged. Thirty-five (6.9%) patients had transient hemoptysis and four (0.8%) had a vasovagal reaction that was unrelated to pneumothorax. These patients were treated with intravenously administered saline with or without atropine.

The time to delayed catheter insertion varied from 3 hours in two patients to 6 days in one. Most patients presented at the emergency department more than 3 hours after biopsy (Table 2). A majority of patients (n = 19) had a catheter placed for 24–48 hours. The longest duration of catheter drainage was 12 days (n = 1).

Table 3 lists the size of the pneumothorax at the time of discharge. These were measured as the distance of the apex of the lung from the first posterior rib. Thirty-two patients were discharged with a pneumothorax 1 cm or less at the apex. Ten patients were discharged with a pneumothorax that extended down to the costophrenic sulcus. Two of these latter patients returned for delayed chest tube insertion.

Eight (1.6%) patients were admitted to the hospital. Four were admitted after immediate catheter insertion: two for pain control possibly related to pleural irritation from the catheter or blood in the pleural space and two for underwater suction to resolve pneumothorax. Three patients who underwent delayed catheter insertion were admitted: one because underwater suction was required and two because a large-bore thoracostomy tube had been inserted at a peripheral hospital. Finally, one patient was admitted for chest pain that was unrelated to pneumothorax.

TABLE 4
Summary of Reported Complication Rates

Study Group	No. of Biopsies	Pneumothorax Rate (%)	Chest Tube Placement Rate (%)
Moore et al, 1990 (4)	308	25.0	1.6
Jereb, 1980 (5)	117	19.0	5.0
Khouri et al, 1985 (10)	650	19.8	5.0
Westcott, 1980 (6)	432	27.0	10.0
Stanley et al, 1987 (12)	458	29.0	10.0
Stevens and Jackman, 1984 (9)	348	41.0	10.0
Perlmutt et al, 1986 (11)	673	23.8	11.5
Jackson et al, 1980 (7)	229	44.0	12.0
Gibney et al, 1981 (8)	146	30.1	14.3

TABLE 5
Summary of Reported Chest Radiographic Follow-up and Discharge

Study Group	Chest Radiography after Biopsy	Discharge Time after Biopsy (h)
Stevens and Jackman, 1984 (9)	Immediately, 1, 24 h	1
Westcott et al, 1997 (21)	1½ h	1½
Westcott, 1988 (19)	15–30 min, 2 h	2
Weisbrod, 1990 (17)	2 h	2
Engeler et al, 1992 (20)	Immediately, 2 h	2
Perlmutt et al, 1986 (11)	1, 4 h	4
Moore et al, 1990 (4)	5–10 min, 1, 2, 3 h	3

DISCUSSION

TTNB of the lung is a commonly performed and widely available procedure associated with very low morbidity and almost no mortality (17). The most common complication is pneumothorax, which is rarely life threatening; the condition usually manifests within 1 hour after the procedure (11) and is readily treatable by the radiologist (18). Table 4 summarizes selected studies in which investigators addressed the problems of postbiopsy pneumothorax and chest tube insertion. The incidence of pneumothorax ranges from 19% to 44%, and the rate of chest tube insertion varies from 1.6% to 14.3%. Table 5 lists a time range of 1–4 hours for discharge after biopsy.

Perlmutt et al (11) studied the time to detection of pneumothorax after lung biopsy. Their rate of pneumothorax was 23.8%. Eighty-nine percent of pneumothoraces were detected immediately after biopsy, with only 2% detected 4 hours after biopsy. They noted that no clinically important pneumothorax was detected after 1-hour chest radiography. We are not aware of other studies in which the time to development of a pneumothorax was specifically assessed.

In their study of 447 biopsies, Stevens and Jackman (9) obtained immediate and 1- and 24-hour postbiopsy chest radiographs. They did not publish exact numeric results but stated that a pneumothorax developed only rarely after 1-hour chest radiography and that although the size of the pneumothorax enlarged between 1- and 24-hour chest radiography in 43% of patients, only a few required chest tube placement at 24 hours. In 1996, Kazerooni and colleagues (22) published a study on the risk of pneumothorax in 121 CT-guided lung biopsies. Their pneumothorax rate was 44.6%, and they obtained chest radiographs 1 and 3 hours after the procedure. Ninety-one percent of pneumothoraces were depicted on the 1-hour chest radiograph, and 9% were depicted on only the 3-hour postbiopsy chest radiograph. None of the pneumothoraces detected 3 hours after biopsy required chest tube insertion.

Moore (14) must be commended for obtaining such a low pneumothorax and chest tube insertion rate (12% and 1%, respectively). The study protocol consisted of performing 1- and 2-hour postprocedure chest radiography and keeping the patient in the biopsy-side-down position until after the second radiographic examination was performed. Then 3-hour postbiopsy radiography was performed after allowing the patient to resume regular activity. The patient was discharged if there was no pneumothorax. This approach definitely yielded a lower pneumothorax and chest tube insertion rate, but many patients at Moore's institution, especially obese patients and patients with moderate to severe emphysema, had difficulty lying in a prone position for a prolonged time after anterior-approach biopsy. These patients seemed to make up most of Moore's biopsy population.

In the current study, patients were discharged 30 minutes after biopsy if there was no pneumothorax and 60 minutes after biopsy if there was a stable asymptomatic pneumothorax. Of note, the patients included in the current study were referred from a surrounding geographic area of up to 120 miles. Only seven, or 1.4%, of the patients had delayed pneumothoraces that required catheter drainage. All except three of the patients were aware of a pneumothorax at discharge. There was no tension pneumothorax or death related to the procedure.

On occasion, the pneumothorax enlarged slightly between 30- and 60-minute radiography. Patients with such enlargements underwent radiography every 30 minutes until the pneumothorax stabilized or the patient developed symptoms.

Eleven patients underwent 90-minute postbiopsy chest radiography: Two subsequently underwent chest tube insertion, and nine were subsequently discharged without a chest tube. One patient was kept 2 hours after biopsy with a pneumothorax that stabilized between 90- and 120-minute postbiopsy chest radiography, only to return the same

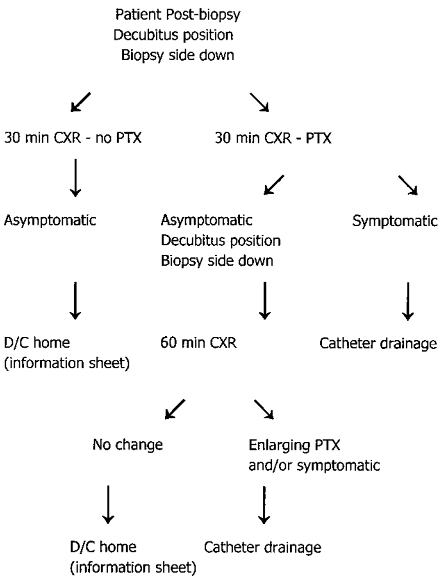


Figure 2. Flow chart shows the proposed patient treatment algorithm after lung biopsy. *CXR* = chest radiograph, *D/C* = discharged, *PTX* = pneumothorax.

evening for delayed chest tube insertion. In general, a pneumothorax was treated if the patient had symptoms, but if the pneumothorax extended down to the costophrenic sulcus in a patient without symptoms who lived more than 30 minutes from the nearest hospital, a catheter was inserted unless the patient could stay nearby overnight. Patients with severe emphysema were treated in the same manner as those without. However, these patients tended to develop symptoms with a much smaller pneumothorax than those without emphysema.

TTNB of pulmonary lesions is a safe and accurate procedure with minimal complications, as compared with those of thoracotomy (2%–3% mortality for lobectomy, and 1%–2% mortality for open biopsy) or video-assisted thoracoscopic surgery (<1% mortality) for diagnosis. At our institution, all patients with focal parenchymal lesions more than 5 mm in diameter and suspicious for cancer or requiring a tissue diagnosis undergo FNAB and/or core biopsy before more invasive procedures are performed. We attempt to make the procedure as innocuous and non–anxiety provoking as possible for patients.

One of the limitations of this study was that there was no control group in which a more traditional 1–2-hour postbiopsy observation period could have been compared with one of 30 minutes; in such a case, the two patients who returned 3 hours after biopsy for delayed catheter insertion might have avoided the inconvenience. The pneumothorax rate of 22.9% might also have been higher if patients had undergone radiography more than 1–2 hours after biopsy rather than only 30 minutes after biopsy. Finally, discharging patients earlier after biopsy may depend on the comfort level of the radiologist who is performing the procedure. Early discharge saves only the cost of two or three additional chest radiographs. However, it enables more flexibility in scheduling the procedures. In our institution, biopsies are performed in the afternoon, without incurring additional costs for keeping nurses and/or radiologic technologists overtime to monitor patients after biopsy and perform chest radiography. In this way, procedures that require patient fasting may be performed in the morning in the same room.

The results of the current study show that an observation period of 30 minutes after lung biopsy can be sufficient for those patients without a pneumothorax. Our postbiopsy patient treatment algorithm for outpatient lung biopsy is shown in Figure 2: A 30-minute postbiopsy chest radiograph is obtained; if there is no pneumothorax and the patient has no symptoms, the patient is discharged with an information sheet. If the patient has a pneumothorax and symptoms, an 8-F catheter is placed, and the patient is discharged with 24-hour outpatient follow-up until the air leak stops. For those patients experiencing pleuritic chest pain that is unrelated to pneumothorax, appropriate analgesics are given, and the patient is observed until the pain resolves and is then discharged. If there is a pneumothorax and the patient has symptoms, a second chest radiograph is obtained 60 minutes after biopsy. If the pneumothorax is stable in size on the 60-minute postbiopsy chest radiograph and the patient remains symptom free, he or she is discharged with an information sheet. However, if the pneumothorax has markedly enlarged and/or the patient has developed symptoms at the time of 60-minute chest radiography, a catheter is placed, with 24-hour outpatient follow-up.

In summary, the findings of the current study illustrate that discharge 30 minutes after lung biopsy in the absence of pneumothorax is a safe approach to the performance of outpatient TTNB of the lung.

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Timing of Chest Film Follow-Up After Transthoracic Needle Aspiration

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Transthoracic needle aspiration of pulmonary lesions is an extremely common procedure. Pneumothorax, the most common complication, is potentially life threatening. In an effort to determine the optimum time for obtaining chest radiographs to detect pneumothorax, all cases of pneumothorax that occurred after transthoracic needle aspiration between 1981 and 1984 were reviewed. During this period, 673 transthoracic-needle-aspiration procedures were performed. Pneuomothorax occurred in 160 patients (23.8%), and 78 (11.5%) of these required a chest tube or aspiration. Of the total number of pneumothoraces, 142 (89%) were detected immediately, 15 (9%) were first seen after 1 hr, and only 3 (2%) were first seen on the 4-hr radiograph. Of the pneumothoraces requiring intervention, 69 (88%) were detected immediately while the remainder were first picked up after 1 hr. There were no significant pneumothoraces detected after the 1-hr radiograph. Immediate fluoroscopy and a routine chest radiograph 1-hour postprocedure are recommended. For outpatients 1-hr and 4-hr follow-up radiographs should be taken.

Transthoracic needle aspiration (TTNA) is an efficient means of obtaining a tissue or culture diagnosis of a wide variety of pulmonary lesions and has become an extremely common intervention procedure. Pneumothorax is the most common and potentially serious complication, occurring in approximately 30% of cases. Despite this frequency, there is no uniform approach to the follow-up of pneumothorax after TTNA. It is the purpose of this study to determine when, after TTNA, most pneumothoraces occur so that one may monitor their resolution and determine whether treatment is required.

Materials and Methods

A total of 673 consecutive patients at Duke University Medical Center underwent TTNA between 1981 and 1984. Reports of this group were retrospectively examined, and those patients in whom pneumothorax was listed as a complication were included in the study. All chest radiographs relating to the procedure were then examined, and the time at which pneumothorax of any size was first detected was recorded.

Aspiration procedures used for TTNA have remained constant during this period. Lesions were routinely aspirated with a 22-gauge thin-walled (Chiba, Medi-Tech, Watertown, MA) needle under biplane fluoroscopic guidance. The chest radiographs, posteroanterior and lateral, were used to determine the optimal (usually shortest) path to the lesion. If the lesion was not seen on the lateral radiograph, a limited CT examination was used for this purpose. A single pass was made and a sample aspirated for cytologic and/or bacteriologic examination. If the initial cytology was acellular (as determined by cytopathology examination), a second pass was made. Immediately after the first aspiration, an upright posteroanterior expiratory chest radiography was obtained. Subsequent radiographs were obtained 1 hr and 4 hr later.

Any evidence of lung collapse was interpreted as pneumothorax. A significant pneumothorax was one in which the attending radiology staff believed intervention by either simple aspiration or placement of a chest tube was needed and that collapse of the lung was usually 30% or more. If a pneumothorax was first detected at any point, and was not felt to be

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significant, a follow-up radiograph was generally obtained about 4 hr later. If comparison of the original and follow-up radiographs showed that the pneumothorax was stable, a final radiograph was obtained the following morning. If there was an increase in size of the pneumothorax or the patient became symptomatic, a chest tube was inserted. Outpatients who developed pneumothoraces were admitted and were followed in the same manner. Outpatients in whom a 4-hr radiograph failed to reveal a pneumothorax were discharged with instructions to return if they became symptomatic.

Results

Of the 673 patients who underwent TTNA, pneumothoraces were detected in 160 (23.8%). The pneumothorax was classified as significant in 78 (48.8% of the 160 cases of pneumothorax or 11.6% of the total group). These patients had immediate evacuation of the pneumothorax by either needle aspiration or, more commonly, insertion of a small, dart-type chest tube.

Of the total number of pneumothoraces, 142 (89%) were first detected on the immediate radiograph; 15 (9%) were initially seen on the 1-hr radiograph; and only 3 (2%) were first seen on the 4-hr radiograph. Of the significant pneumothoraces, 69 (88%) were detected immediately, while the rest were first identified on the 1-hr radiograph. No significant pneumothoraces were first detected after the 1-hr radiograph. In no case was a chest tube placed for a delayed symptomatic pneumothorax.

Discussion

TTNA has proved to be an extremely useful procedure for the evaluation of a variety of lung disease. Its most common and potentially serious complication is pneumothorax. The development of pneumothorax after TTNA has been attributed to a number of factors, including the size of the needle used, the number of times the visceral pleura is punctured, and the presence or absence of obstructive lung disease [1]. The incidence of pneumothorax after TTNA as reported in the literature ranges from 5% to 57%, with 2% to 17% requiring a chest tube [2–4]. Even with the use of smaller (22-gauge) needles, the frequency of pneumothorax has not decreased [5].

In general, the population of patients undergoing TTNA belongs to an older age group, has a higher frequency of smoking and chronic lung disease, and thus has a limited respiratory reserve. It is in this group that pneumothorax is least well tolerated. For example, in two series, 10 (18%) of 57 and 12 (16%) of 74 patients with pneumothorax (from various causes) died [6, 7]. It is, therefore, essential to detect the presence of pneumothorax in a timely and efficient manner.

In spite of this frequent and potentially dangerous complication, there is no uniform method of surveillance for the detection of pneumothorax after TTNA. Johnson et al. [8] recommend a follow-up chest radiograph immediately after the procedure and a repeat radiograph if clinically indicated. For outpatients, radiographs are taken immediately and after 4 hr. Gibney et al. [9] suggest a follow-up radiograph the morning after the procedure. Youmans et al. [10] placed a chest tube after biopsy of diffuse parenchymal disease in each patient and obtained radiographs on the evening of the study.

It has been estimated that most pneumothoraces occur within 30 min after the procedure and that some with a small leak may not become evident for 3 or 4 hr [1]. Stevens and Jackman, from their experience in performing a large series of outpatient TTNAs, state that rarely did pneumothorax become apparent after the first hour of observation [11]. Our study supports these statements. Of the total number of pneumothoraces, 98% were first detected within 1 hr after the procedure, while only 2% were first seen on delayed radiographs. However, of the significant pneumothoraces, all were discovered within 1 hr after TTNA.

We recommend chest fluoroscopy after the TTNA. This should be adequate to detect large pneumothoraces and is easily done. A chest radiograph obtained 1 hr after the procedure will detect 98% of pneumothoraces and identify all of those requiring intervention. For outpatients, a 4-hr radiograph is also obtained. The relatively few patients in whom a significant pneumothorax may occur after this time should be clinically apparent.

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Incidence and Risk Factors of Delayed Pneumothorax After Transthoracic Needle Biopsy of the Lung*

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Study objectives: **To evaluate the incidence and clinical significance of delayed pneumothorax, and to analyze the influence of multiple variables on the rate of delayed pneumothorax associated with transthoracic needle biopsy (TTNB) of the lung.**
Study design: **Prospective study.**
Setting: **Tertiary care university hospital.**
Study subjects: **Adult patients underwent TTNB from June 2001 to June 2002.**
Measurements and results: **Among the 458 patients included in this study, 280 fluoroscopic-guided, 21 CT-guided, and 157 ultrasonography-guided lung biopsies were performed. A follow-up chest radiograph was obtained immediately, and 3 h, 8 h, and 24 h after the biopsy procedure. Pneumothorax that had not developed up to 3 h but developed later was defined as a delayed pneumothorax. Patients with a symptomatic or enlarged pneumothorax were treated using a pigtail catheter or chest tube. Variables such as age, gender, lesion size, location, presence of an emphysematous change, biopsy guidance methods, and biopsy devices were analyzed. Pneumothorax developed in 100 of the 458 patients (21.8%), and delayed pneumothorax developed in 15 patients (3.3%). Seventeen patients, including 3 patients with delayed pneumothorax, required a pigtail catheter or a chest tube insertion. The pigtail catheter or chest tube insertion rate in delayed pneumothorax was 20% (3 of 15 patients). Female gender and the absence of an emphysematous change correlated with an increased rate of delayed pneumothorax ($p < 0.05$). Lesion size, location, biopsy guidance methods, devices, and underlying diseases were not correlated with the delayed pneumothorax rate.**
Conclusions: **The incidence of delayed pneumothorax was 3.3% of all TTNBs. Female gender and the absence of an emphysematous change were identified as risk factors for delayed pneumothorax. Delayed pneumothorax is clinically important because of its considerable incidence and the necessity for pigtail catheterization or chest tube insertion in these patients.**
(CHEST 2004; 126:1516–1521)

Key words: complication; delayed pneumothorax; emphysema; transthoracic needle biopsy of lung

Abbreviations: PA = posteroanterior radiograph; PACS = picture archiving and communication system; TTNB = transthoracic needle biopsy

Transthoracic needle biopsy (TTNB) of the lung is a well-established and effective method for obtaining pulmonary tissue for pathologic examination.[1–3] Although it is generally a safe and well-tolerated procedure, pneumothorax is a relatively common and there are potentially serious complications.

The reported incidence of pneumothorax as a complication of TTNB varies widely from 8 to 61%, with a 10.4 to 17.4% chest tube insertion rate.[1,2,4,5] Because pneumothorax usually occurs immediately, a further 9% are detected by chest radiography 1 h after biopsy, and an additional 2% are detected at 4 h.[4,6] Early hospital discharge after TTNB has been recommended by previous studies.[7–9] However, it is not well known how often pneumothorax presents as a late complication. The reported incidence of delayed pneumothorax varies from 1.4 to 4.5%.[8–10]

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Therefore, operators' concerns about potential delayed pneumothorax have lead some clinicians to request postprocedure chest radiographs.[11]

Our institute has performed TTNB on inpatients for a long time, and we have found that delayed pneumothorax is not a rare event. Therefore, we performed this prospective study to analyze the incidence, risk factors, and clinical significance of delayed pneumothorax.

Materials and Methods

Study Design

From June 2001 to June 2002, we conducted a prospective study of 458 patients who underwent TTNB. Two hundred eighty biopsies (61.1%) were performed with fluoroscopic guidance, 21 biopsies (4.6%) were performed with CT guidance, and 157 biopsies (34.3%) were performed with ultrasonographic guidance. Coaxial procedures were performed using an 18-gauge TSK gun (TSK Laboratory; Tochigi, Japan). A biopsy of a peripheral lesion was often performed directly using a 22-gauge needle (Westcott needle; Medical Device Technologies; Gainesville, FL).

The procedure was performed with the patient in a prone, supine, or lateral decubitus position, depending on the location of the lesion. Pleural effusions, fissures, and bullae were avoided during biopsy if possible.

After biopsy, all patients were placed in the decubitus position to compress the biopsy site. To confirm the occurrence of pneumothorax, chest posteroanterior radiographs (PAs) using a digital imaging system and displayed by a picture archiving and communication system (PACS) were obtained immediately, and 3 h, 8 h, and 24 h after TTNB in the erect position. The presence of pneumothorax was thoroughly investigated by using a magnifier on the PACS. If the patient complained of symptoms related with possible complications (pneumothorax or hemoptysis), a chest PA was obtained. If pneumothorax was detected on later chest PAs, previous chest PAs were scrutinized for previously undetected pneumothorax using the PACS magnifier.

Data Analysis

Demographic information including patient's age and gender, lesion size and location, number of pleural punctures, types of devices used, and the presence or absence of emphysematous change in same lobe in which biopsy was obtained were analyzed. The presence of any type of emphysema in the lobe in which biopsy was performed was determined by high-resolution chest CT imaging in all patients. All chest radiographs and chest CTs were examined by at least one radiologist and one pulmonologist, and all complications including pneumothorax, the necessity for catheter insertion, and accompanying symptoms were recorded.

Pneumothorax that developed > 3 h after TTNB was defined as delayed pneumothorax. Pneumothorax that developed immediately or up to 3 h after TTNB was defined as an early pneumothorax. Patients with stable, asymptomatic pneumothorax were closely observed with oxygen inhalation. Patients with a large pneumothorax underwent immediate needle aspiration. The indications for catheter insertion were as follows: (1) a large pneumothorax (> 35% apical or when smaller with a lateral thoracic component extending below the level of the hilum), (2) progressive pneumothorax (increasing in size on following radiographs indicating a continuous leak), and (3) symptomatic patients (severe pain or dyspnea).

Statistical Analysis

Statistical analysis was performed using commercially available software (SPSS 10.0 for Windows; SPSS; Chicago, IL). Quantitative variables were compared using the unpaired t test, and qualitative variables were compared using the χ^2 test.

Results

Characteristics of Study Population and Diseases

Four hundred fifty-eight patients (279 men and 179 women) were included in the study. Mean patient age was 59 years (range, 19 to 90 years). The average lesion diameter was 3.31 cm (range, 0.5 to 11.0 cm). Four hundred nine patients had no visible emphysematous change by chest CT, and 70 patients showed emphysematous change in the same lobe of the lesion. Table 1 summarizes the demographic data and multiple variables in the 458 patients.

Incidence and Characteristics of Pneumothorax

Pneumothorax occurred in 100 of the 458 patients (21.8%). Delayed pneumothorax was found in 15 cases (15% of pneumothorax and 3.3% of total procedures). Three of the 15 cases (20%) of delayed pneumothorax required chest tube placement.

Female gender was found to be related to delayed pneumothorax. Of the 458 patients, 179 were women and 279 were men. Delayed pneumothorax occurred in 10 of the 179 female patients and in 5 of the 279 male patients ($p = 0.046$), and this gender difference was statistically significant. However, female gender was not a risk factor for the development of early pneumothorax ($p > 0.05$). The lesion size in patients with delayed pneumothorax (2.47 ± 1.14 cm [mean $\pm$ SD]) was significantly smaller than in patients without pneumothorax (3.46 ± 1.87 cm) [$p < 0.05$], and lesion size in patients with early pneumothorax was also significantly smaller than in patients without pneumothorax ($p < 0.05$). No difference in lesion size was found between early and delayed pneumothorax. Therefore, a small lesion was identified as a risk factor of early and delayed pneumothorax.

Fine-needle aspiration biopsy (22-gauge Westcott needle) was performed in 417 procedures (91.0%), gun biopsy (18-gauge TSK gun) was performed in 14 procedures, and both fine-needle aspiration biopsy and gun biopsy were performed in 27 procedures (5.9%). The use of a larger (18-gauge) needle was not found to be a significant risk for pneumothorax compared with the smaller (22-gauge) needle.

Another important risk factor was the presence of emphysematous change in the same lobe. The presence of emphysematous change was identified as a

Table 1—*Incidence of Pneumothorax in Patients Undergoing TTNB

Variables	No Pneumothorax	Early Pneumothorax	Delayed Pneumothorax	Total
Patients, No.	358	85	15	458
Age, yr	58.8 ± 12.3	59.0 ± 12.7	55.7 ± 10.3	58.8 ± 12.3
Male/female gender, No.	212/146	63/23†	5/10‡§	279/179
Lesion size, cm	3.5 ± 1.9	2.8 ± 1.5†	2.5 ± 1.1‡	3.3 ± 1.8
Lesion location				
Right upper	102 (28.5)	24 (28.2)	5 (33.3)	131
Right middle	26 (7.3)	7 (8.2)	0 (0)	33
Right lower	81 (22.6)	18 (21.2)	3 (20.0)	102
Left upper	83 (23.2)	23 (27.1)	5 (33.3)	111
Left lower	66 (18.4)	13 (15.3)	2 (13.3)	81
Emphysema in some lobe of lesion	23 (6.4)	26 (30.6)†	0 (0)§	49 (10.7)
Guidance methods				
Fluoroscopic	214 (59.8)	58 (68.2)†	8 (53.3)	280
CT	12 (3.4)	9 (10.6)	0 (0)	21
Ultrasonographic	132 (36.9)	18 (21.2)	7 (46.7)	157
Device				
Needle	324 (90.5)	79 (92.9)	14 (93.3)	417
Gun	12 (3.4)	2 (2.4)	0 (0.0)	14
Needle plus gun	22 (6.1)	4 (4.7)	1 (6.7)	27
Diagnosis				
No diagnosis	112 (31.3)	36 (42.4)	5 (33.3)	153
Malignancy	185 (51.6)	34 (40.0)	7 (46.7)	226
Metastasis	17 (4.7)	4 (4.7)	2 (13.3)	23
Benign	9 (2.5)	2 (2.4)	0 (0)	11
Tuberculosis	23 (6.4)	8 (9.4)	1 (6.7)	32
Infection	12 (3.4)	1 (1.2)	0 (0)	13
Treatment				
Tube insertion	0 (0)	14 (16.5)	3 (20.0)	17

*Data are presented as mean ± SD or No. (%) unless otherwise indicated.
†Significant difference compared with patients without pneumothorax ($p < 0.05$).
‡Significant difference compared with patients without pneumothorax ($p < 0.05$).
§Significant difference compared with patients with early pneumothorax ($p < 0.01$).

definite risk factor of pneumothorax ($p < 0.005$): 26 pneumothoraces (53.0%) among 49 emphysematous lungs vs 74 pneumothoraces among 409 nonemphysematous lungs.

Interestingly, emphysematous lung was not observed in the 15 delayed pneumothorax cases, compared with 26 emphysematous lungs (30.5%) in 85 cases of early pneumothorax ($p < 0.01$). In other words, all cases of delayed pneumothorax developed in a lung without emphysematous change. Therefore, the absence of an emphysematous change was identified as a risk factor of delayed pneumothorax as compared with early pneumothorax.

In patients with pneumothorax, the frequency of chest tube placement was not significantly different (16.5% in early and 20% in delayed pneumothorax). The time to detect delayed pneumothorax varied from 5 to 120 h. Six patients (40%) with delayed pneumothorax complained of chest symptoms at the time of chest PA; however, no symptoms developed in 60% of the patients with delayed pneumothorax. Three of the six symptomatic patients underwent catheter placement. The time to catheter insertion in delayed pneumothorax varied from 56 to 120 h (Table 2; Fig 1, 2).

In one 75-year-old patient (Table 2; case 3), mild dyspnea developed at 17 h after TTNB, and no evidence of pneumothorax was found by chest PA at 24 h. The patient received oxygen therapy only up to 120 h, until pneumothorax was detected with increasing dyspnea (Fig 2). This symptom was due to a total left pneumothorax and a hemothorax not visible on earlier chest radiographs. This patient required chest tube insertion and emergent bronchial arterial embolization due to massive bleeding in the pleural cavity.

Discussion

TTNB of the lung has proven to be an extremely useful procedure for the evaluation of a variety of lung diseases,[1–3] and the most common and potentially serious complication of TTNB is pneumothorax. The reported incidence of pneumothorax as a

Table 2—*Characteristics of 15 Delayed Pneumothorax Cases After TTNB*

Patient No.	Gender/ Age, yr	Lesion Size, cm	Lobe	Emphysema	Guidance Methods	Device	Diagnosis	Symptom Onset, h	Chest Tube Insertion, h
1	Male/59	2.5	Right upper	Absent	Ultrasonography	Needle	Lung cancer	56	56
2	Male/50	2	Left upper	Absent	Ultrasonography	Needle	Lung cancer	57	57
3	Male/75	3.2	Left lower	Absent	Fluoroscopy	Needle	Metastasis	17	120
4	Female/60	2	Right upper	Absent	Ultrasonography	Needle	Tuberculosis	0	
5	Female/37	2.5	Right upper	Absent	Fluoroscopy	Needle plus gun	Metastasis	0	
6	Female/64	1	Right upper	Absent	Ultrasonography	Needle	Lung cancer	0	
7	Female/55	5	Left upper	Absent	Fluoroscopy	Needle	Lung cancer	0	
8	Male/60	2	Right lower	Absent	Ultrasonography	Needle	No diagnosis	15	
9	Female/42	4.5	Right upper	Absent	Fluoroscopy	Needle	Lung cancer	0	
10	Female/62	2.5	Right lower	Absent	Fluoroscopy	Needle	Lung cancer	0	
11	Female/46	2.5	Left upper	Absent	Ultrasonography	Needle	No diagnosis	0	
12	Male/54	1.3	Right lower	Absent	Fluoroscopy	Needle	No diagnosis	0	
13	Female/63	3.1	Left upper	Absent	Fluoroscopy	Needle	Lung cancer	5	
14	Female/65	1	Left upper	Absent	Ultrasonography	Needle	Metastasis	0	
15	Female/43	2	Left lower	Absent	Fluoroscopy	Needle	No diagnosis	6	

complication of percutaneous lung biopsy varies widely from 8 to 61%, with a 10.4 to 17.4% chest tube insertion rate.[1,2,4,5]

It has been estimated that most cases of pneumothorax occur within 30 min of the procedure, and that some with a small leak may not become evident for 3 h or 4 h.[4,6] In a study by Perlmutt et al[4] of 673 patients who underwent percutaneous TTNB, no pneumothoraces developed > 4 h after the procedure, and it was recommended that chest radiographs be obtained at 1 h and 4 h after biopsy in outpatients. Therefore, TTNB is routinely performed as an outpatient procedure.[7,9,12] Stevens and Jackman,[7] based in their experience of performing a large series of TTNBs in an outpatient setting, found that pneumothorax rarely became apparent after the first hour of observation. Dennie et al[9] concluded that early discharge (30 min) after lung biopsy in the absence of pneumothorax was a safe approach to outpatient TTNB.

However, it is not well known how often pneumothorax presents as a late complication. The reported incidence of delayed pneumothorax varies from 1.4 to 4.5%.[8–10] The substantial incidence of delayed

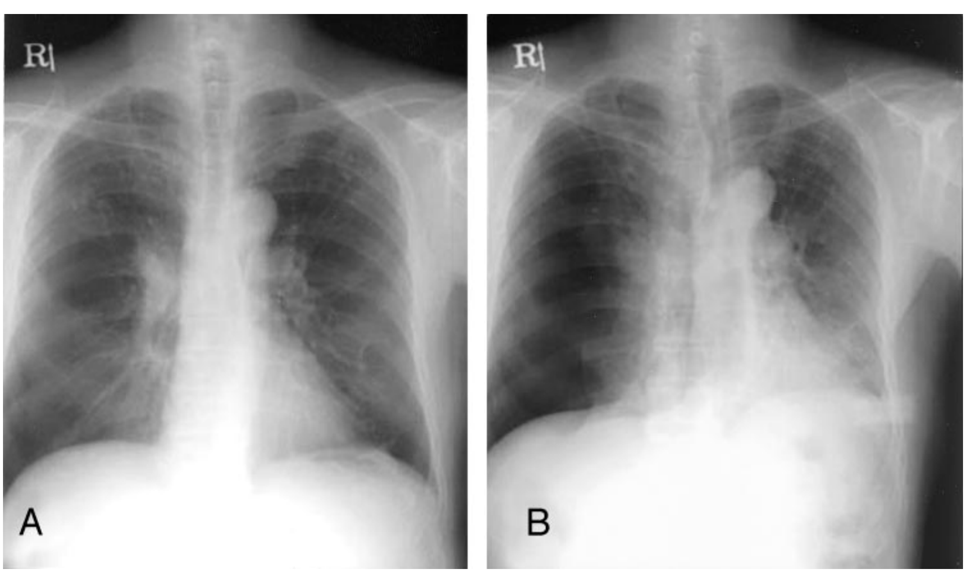

FIGURE 1. Delayed pneumothorax (case 2). *Left*, *A*: Chest PA obtained 3 h after TTNB. No evidence of pneumothorax was found. *Right*, *B*: Chest PA obtained 57 h after TTNB. A large pneumothorax on right lung and shifting of mediastinal structures were found. A chest tube was inserted to relieve dyspnea.

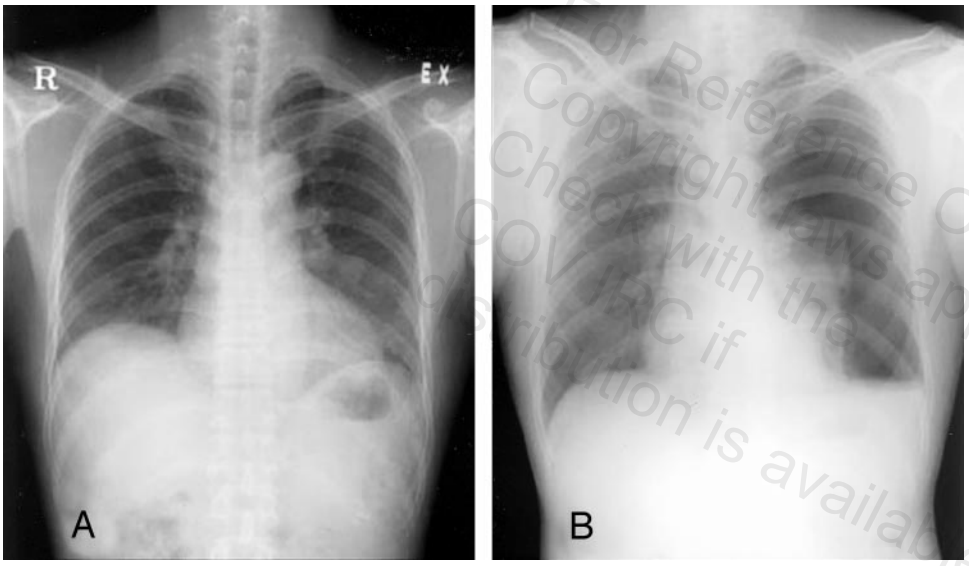

FIGURE 2. Delayed pneumothorax (case 3). *Left*, *A*: Chest PA obtained 3 h after TTNB. No evidence of pneumothorax was found. *Right*, *B*: Chest PA obtained 120 h after TTNB. Total lung collapse and fluid level were found. A chest tube was inserted to relieve dyspnea.

pneumothorax and the potential hazards of undetected pneumothorax leads some clinicians to request postprocedure chest radiographs for > 4 h.[11] Traill and Gleeson[13] reported two patients who acquired pneumothorax > 24 h after CT-guided TTNB; the pneumothorax required treatment in both cases. Delayed pneumothorax has been also reported as a complication of transbronchial lung biopsy,[14] and of subclavian vein catheterization.[15,16]

Our prospective study shows that the delayed pneumothorax rate was 3.3% (15 of 496 procedures) in 458 patients who underwent biopsy. The development of pneumothorax after TTNB has been attributed to a number of factors, including the lesion size and the location and presence of emphysema.[5] Cox et al[5] found that a smaller lesion size and emphysema were strongly correlated with the occurrence of pneumothorax, and used thin-section CT to determine if emphysema was visible in the lobe in which the biopsy was performed. We also found a significantly higher ($p < 0.001$) risk of early pneumothorax in patients with emphysema. In contrast, the absence of an emphysematous change was found to be a risk factor of delayed pneumothorax. In patients with emphysema, the disruption of dilated air spaces and the lack of elastic recoil may prevent rapid sealing of the air leak.[17] Because pneumothorax occurs more quickly in patients with emphysema, delayed pneumothorax rarely develops. However, the elastic recoil of the normal lung parenchyma and pleura over the lesion may seal the small opening of the pleura initially to prevent early pneumothorax. Thus, the later weakening of elastic recoil may facilitate delayed pneumothorax.

The strong correlation between the pneumothorax rate and lesion size is difficult to explain, although this correlation has been previously reported.[5,17] A possible explanation for this finding is that the up-and-down movement of the needle tip during aspiration biopsy results in more tearing of adjacent lung parenchyma when the lesion is relatively small.[5]

Every patient undergoing this procedure should be warned of the importance of seeking medical attention should increased breathlessness or chest pain develop, and urgent chest radiographic examinations should be performed in all patients with acute respiratory symptoms. We detected three cases of significant delayed pneumothorax requiring immediate chest tube insertion. They were detected at 56 h, 57 h, and 120 h after TTNB, respectively, and showed no evidence of pneumothorax on a 3-h postprocedure radiograph. The relation between TTNB and pneumothorax is not clear, but the lack of other risk factors strongly suggests a causal relationship.

The reason and mechanism of the delayed presentation of pneumothorax is not clear. We reviewed the clinical records of the patients with delayed pneumothorax, and we were unable to find any procedure, such as pulmonary function testing, contributing to pneumothorax. Six patients (40%) with delayed pneumothorax were symptomatic (dyspnea, cough, chest pain); however, it was not clear whether these symptoms were the cause or the result of the delayed pneumothorax.

Because some patients had a history of sudden exertion or coughing prior to the onset of symptoms, delayed pneumothorax might be related to the dis-

placement of small pleural blood clots formed after the biopsy procedure. Pneumothorax could have occurred after fibrinolysis,[14] and delayed pneumothorax may have been caused by a slow pleural air leak associated with the insertion.[15,16,18]

In summary, the incidence of delayed pneumothorax was 3.3% among all percutaneous lung biopsies. Delayed pneumothorax was more frequent in female patients and in underlying normal lung parenchyma in contrast to early pneumothorax. This condition is clinically significant, because 20% of patients with delayed pneumothorax required pigtail catheterization or chest tube insertion. Although the incidence of delayed pneumothorax is low, it is potentially life threatening, and a high index of suspicion is required to properly diagnose and treat this reversible condition. Most cases of delayed pneumothorax occur within 24 h, however, delayed pneumothorax developed after 24 h in 3 of our 15 delayed pneumothorax cases. So we advise patients to bear in mind the possibility of pneumothorax, and to visit the emergency department if dyspnea develops. In addition, we recommend that a chest PA be obtained up to 24 h after TTNB.

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Risk Factors for Severity of Pneumothorax after CT-Guided Percutaneous Lung Biopsy using the Single-Needle Method

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ABSTRACT

The purpose of this study is to evaluate the risk factors for the severity of pneumothorax after computed tomography (CT)-guided percutaneous lung biopsy using the single-needle method. We reviewed 91 biopsy procedures for 90 intrapulmonary lesions in 89 patients. Patient factors were age, sex, history of ipsilateral lung surgery and grade of emphysema. Lesion factors were size, location and pleural contact. Procedure factors were position, needle type, needle size, number of pleural punctures, pleural angle, length of needle passes in the aerated lung and number of harvesting samples. The severity of pneumothorax after biopsy was classified into 4 groups: "none", "mild", "moderate" and "severe". The risk factors for the severity of pneumothorax were determined by multivariate analyzing of the factors derived from univariate analysis. Pneumothorax occurred in 39 (43%) of the 91 procedures. Mild, moderate, and severe pneumothorax occurred in 24 (26%), 8 (9%) and 7 (8%) of all procedures, respectively. Multivariate analysis showed that location, pleural contact, number of pleural punctures and number of harvesting samples were significantly associated with the severity of pneumothorax ($p<0.05$). In conclusion, lower locations and non-pleural contact lesions, increased number of pleural punctures and increased number of harvesting samples presented a higher severity of pneumothorax.

Key words: *Complication, Computed tomography (CT), Biopsy, Lung*

CT-guided percutaneous lung biopsy is a well-established procedure that is safe and well-tolerated for diagnosing lung lesions[2, 4, 7, 8, 11, 14, 15]. However, pneumothorax occurs frequently as a complication of the procedure, of which the reported rate is from 8 to 45%[2-4, 6, 8-13, 15]. Although, in the majority of cases, pneumothorax is asymptomatic and resolves spontaneously, a small number of patients with a large pneumothorax require chest tube placement. The rate of pneumothorax requiring chest tube placement varies widely from 0 to 33%[1-6, 8-14]. There are many reports investigating the risk factors that influence any pneumothorax[2-5, 8, 9, 11, 13-15] and the requirement of chest tube placement[2, 3, 5, 7-10]. The reported risk factors for requiring chest tube placement are longer length of needle passes in the aerated lung, wider pleural angle, severe emphysema, obstructive lung disease and hyperinflation[3, 5, 7-10]. Unfortunately, these risk analyse of pneumothorax and chest

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tube placement are variable and often times contradictory. Indications of the need for chest tube placement, such as signs of respiratory distress, shortness of breath, large pneumothorax or markedly enlarging pneumothorax[2, 4, 5, 8-11, 13, 15], are necessarily subjective depending on the observer.

In this study, we evaluated objectively the risk factors that influence the severity of pneumothorax after lung biopsy. This evaluation may be useful for risk management in CT-guided percutaneous lung biopsy.

MATERIALS AND METHODS

Patient Population

From August 2000 to May 2006, ninety-five consecutive CT-guided percutaneous lung biopsies for 95 lung lesions in 91 patients were performed at Hiroshima University Hospital. Two biopsies were performed for 2 coexistent lesions in 2 patients in one session. These procedures were excluded from evaluation in this study. Repeat biopsy for one lesion in one patient and two biopsies for two different lesions in one patient, in another session, were performed, respectively. Each procedure was calculated as a new procedure. As a result, this study included 91 lung biopsy procedures for 90 lung lesions in 89 patients.

The medical charts, radiologic data and pathologic reports for all the procedures were reviewed retrospectively. This study selected only intrapulmonary lesions. Core biopsy, aspiration biopsy, or combinations of these, were used as biopsy techniques, according to the object of histological or cytological diagnoses, and lesion characteristics.

Biopsy Procedures

Written informed consent was obtained before lung biopsy from patients and family members. No institutional review board approval was required. All procedures were performed with hospital admission. A lung function test was not required as our biopsy protocol. As a general rule, biopsy was not refused due to severe emphysema. Our exclusion criteria were: the lesion diameter was less than 5 mm; if the patient had bleeding diathesis, or if the patients could not follow verbal or visual instructions or tolerate recumbent positions. Procedures were performed by one of six interventional radiologists who had over five years experience performing lung biopsy, with direct supervision by one of three experienced interventional radiologists.

All procedures were performed under local anesthesia with CT guidance (SOMATOM Plus4 Volume Zoom; Siemens, Erlangen, Germany) with patients in a prone, supine, or oblique position, depending on the lesion location. 18-21 gauge, half-automated cutting needles (Temno Ⅱ; Allegiance, McGaw Park, IL) for core biopsy and sonopsy needles (PTC needle; Hakko, Chikuma, Japan) for aspiration biopsy were used, respectively. All procedures were prepared by an on-site cytotechnologist, who immediately evaluated the adequacy of harvesting samples.

CT images were obtained using 3-mm section thickness throughout the region of interest. A biopsy needle trajectory was selected to give a short needle path and avoid bullae, fissures and visible vessels whenever possible. By scanning intermittent CT using 2-mm section thickness, the needle was inserted and advanced to an adequate position for the target lesion. The cutting needle for core biopsy was manually pushed into the lung lesion and a fixed 1.0-cm (lesion size < 1.5 cm) or 2.0-cm (lesion size > 1.5 cm) long tissue core was obtained by triggering the spring-loading. The sonopsy needle for aspiration biopsy was inserted into and withdrawn from the lung lesion using a 20 ml syringe for aspiration. Immediately after harvesting a sample, the needle was withdrawn from the pleura. Then, the cytotechnologist visually examined the samples and prepared rapid toluidine blue-stained specimens. When it was considered that the sample was of insufficient quality or the specimen was inadequate (e.g. normal lung cell, blood clot or necrosis) for diagnosis, an additional biopsy was performed, occasionally changing the biopsy types or the needle sizes, if deemed safely feasible for patients. Harvested samples were submitted in 10% formalin for pathologic examination. When clinical or imaging features suggested infection, a section of the sample was also cultured.

Immediately after biopsy, the whole lung CT was examined to check for complications. If CT revealed large pneumothorax, it was aspirated by inserting an 18-gauge intravenous catheter (Surflo; Termo, Tokyo, Japan), regardless of the patient's symptoms (the criteria of severity of pneumothorax for air aspiration was indefinite). After the procedure, all patients were transferred to the clinical department, where they were kept under observation for at least overnight. Asymptomatic patients with no pneumothorax on postbiopsy CT were given bed rest for 2 hr. Patients with any pneumothorax on postbiopsy CT had been given bed rest until the following morning conservatively, and if required, given oxygen inhalation. Routine initial follow-up chest radiographs in the upright position were obtained to evaluate the appearance or enlargement of the pneumothorax the following morning. In some patients with a large pneumothorax on postbiopsy CT, a follow-up chest radiograph or CT was obtained from 2, 4 or 6 hr after the procedure. A chest tube was placed for patients with signs of moderate or severe respiratory symptoms or with a markedly enlarging pneumothorax during observation after procedures. The decision

of the pulmonary physicians (the criteria of chest tube placement was also indefinite). Patients with slight respiratory symptoms, or slight or no enlarging pneumothorax on chest radiographs were conservatively treated continuously, and further follow-up chest radiographs were obtained every 1 to 2 days if needed.

Definition and Data Collection

Table 1-3 shows evaluation factors that influence the severity of pneumothorax.

Patient factors (Table 1) were age, sex, history of ipsilateral lung surgery and grade of emphysema in the needle tract. Age categories were divided into two groups: > 60 y (64 patients: 70%) and > 70 y (36 patients: 40%). There were 65 male patients (71%). There was a history of lung surgery in 7 patients (8%). Grade of emphysema was assessed in the needle tract on CT of 3 mm thickness at the biopsy according to a three-level scale as grade 0-2 by modifying the criteria of Topal, U. et al[11] as follows: "grade 0" if no emphysema (42 patients: 46%), "grade 1" if emphysema affected less than 25% of the lung surrounding the lesion (21 patients: 23%) and "grade 2" if over 25% was affected (28 patients: 31%).

Lesion factors (Table 2) were lesion size, location and pleural contact. Lesion size categories were divided into three groups: ≦ 20 mm (41 lesions: 45%), 21- 40 mm (36 lesions: 40%) and 40 mm < (14 lesions: 15%). Location categories were divided into three groups by trisecting the whole lung field in a cranio-caudal axis by diagnostic CT before biopsy: "upper" (36 lesions: 40%), "middle" (35 lesions: 38%) and "lower" (20 lesions: 28%). Pleural contact was defined as where the length of pleural abutting was over 1 cm. Pleural contact was seen in 58 patients (64%).

Procedure factors (Table 3) were position, needle type, needle size, number of pleural punctures, pleural angle, length of needle passes in the aerated lung and number of harvesting samples. Position categories were divided into two groups: spine (28 procedures: 31%) and prone (63 procedures: 69%), including each oblique position. Needle type categories were 2 different techniques: core biopsy (78/86 procedures: 91%) and aspiration biopsy (8/86 procedures: 9%). A combination of both techniques (5 procedures) was excluded from the analysis. Needle size categories were divided into two groups as 18-19 gauge (26/86 procedures: 30%) and 20-21 gauge (60/86 procedures: 70%), which excluded the combination of these two groups (5 procedures). Number of pleural puncture categories were one (60 procedures: 66%), two (22 procedures: 24%) and above three times (9 procedures: 10%). Pleural angle was measured as the smallest angle formed by a

Table 1. Patient Factors of Severity of Pneumothorax and Univariate Analysis

Patient factors	Severity of pneumothorax				p value
	None (n = 52)	Mild (n = 24)	Moderate (n = 8)	Severe (n = 7)	
Age (y) : Mean 64.6 ± 13.0					
≦60 (n = 27)	15 (56)	7 (26)	3 (11)	2 (7)	0.81*
> 60 (n = 64)	37 (58)	17 (26)	5 (8)	5 (8)	
≦70 (n = 56)	34 (61)	12 (21)	4 (7)	6 (11)	0.64*
> 70 (n = 35)	18 (52)	12 (34)	4 (11)	1 (3)	
Sex					
Male (n = 65)	34 (52)	19 (29)	7 (11)	5 (8)	0.17*
Female (n = 26)	18 (69)	5 (19)	1 (4)	2 (8)	
Prior surgery					
Yes (n = 7)	5 (72)	1 (14)	1 (14)	0 (0)	0.46*
No (n = 84)	47 (56)	23 (28)	7 (8)	7 (8)	
Grade of emphysema					
Grade 0 (n = 42)	22 (52)	13 (31)	3 (7)	4 (10)	0.39**
Grade 1 (n = 21)	12 (57)	5 (24)	3 (14)	1 (5)	
Grade 2 (n = 28)	18 (64)	6 (22)	2 (7)	2 (7)	

Note – Data of factors are presented as mean ± SD.

Severity of pneumothorax is classified into four groups: "none", "mild"; ≦1 cm "moderate"; 1-3 cm and "severe"; ≧ 3 cm, by lung surface retraction from the chest wall.

Numbers in parentheses in severity of pneumothorax are presented percentages (%).

*Mann-Whitney's U test, **Spearman's correlation coefficient by rank test.

Table 2. Lesion Factors of Severity of Pneumothorax and Univariate Analysis

Lesion factors	Severity of pneumothorax				p value
	None (n = 52)	Mild (n = 24)	Moderate (n = 8)	Severe (n = 7)	
Size (mm): Mean 26.6± 15.2					
≦20 (n = 41)	15 (37)	16 (39)	5 (12)	5 (12)	< 0.05**
21 - 40 (n = 36)	25 (69)	6 (17)	3 (8)	2 (6)	
> 40 (n = 14)	12 (86)	2 (14)	0 (0)	0 (0)	
Location					
Upper (n = 36)	26 (72)	5 (14)	5 (14)	0 (0)	< 0.05**
Middle (n = 35)	20 (57)	10 (29)	1 (3)	4 (11)	
Lower (n = 20)	6 (30)	9 (45)	2 (10)	3 (15)	
Pleural contact					
Yes (n = 58)	41 (70)	12 (21)	4 (7)	1 (2)	< 0.05*
No (n = 33)	11 (33)	12 (37)	4 (12)	6 (18)	

Note – * Mann-Whitney's U test. ** Spearman's correlation coefficient by rank test.

Table 3. Procedure Factors of Severity of Pneumothorax and Univariate Analysis

Procedure factors	Severity of pneumothorax				p value
	None (n = 52)	Mild (n = 24)	Moderate (n = 8)	Severe (n = 7)	
Position					
Supine (n = 28)	14 (50)	8 (28)	4 (14)	2 (7)	0.35*
Prone (n = 63)	38 (60)	16 (26)	4 (6)	5 (8)	
Needle type***					
Cutting (n = 78)	44 (56)	20 (26)	7 (9)	7 (9)	0.89*
Aspiration (n = 8)	4 (50)	4 (50)	0	0	
Needle size***					
18 - 19 gauge (n = 26)	17 (65)	6 (23)	1 (4)	2 (8)	0.24*
20 - 21 gauge (n = 60)	31 (52)	17 (28)	7 (12)	5 (8)	
Number of pleural puncture Mean 1.48 ± 0.81					
1 (n = 60)	38 (63)	14 (23)	4 (7)	4 (7)	< 0.05**
2 (n = 22)	11 (50)	8 (36)	2 (9)	1 (5)	
≧ 3 (n = 9)	3 (34)	2 (22)	2 (22)	2 (22)	
Pleuralangle***: Mean 64.5 ± 20.3					
0 – 50° (n = 22)	15 (68)	6 (27)	1 (5)	0 (0)	0.28**
51-70° (n = 20)	11 (55)	5 (25)	2 (10)	2 (10)	
>70° (n = 40)	22 (55)	11 (28)	4 (10)	3 (7)	
Length of needle passes in the aerated lung (mm): Mean 15.3 ± 20.9					
0 (n = 26)	20 (77)	3 (12)	1 (4)	2 (7)	< 0.05**
1 – 20 (n = 37)	22 (60)	11 (30)	2 (5)	2 (5)	
21 - 40 (n = 21)	9 (43)	7 (33)	3 (14)	2 (10)	
> 40 (n = 7)	1 (14)	3 (43)	2 (29)	1 (14)	
Number of harvesting samples: Mean 1.40 ± 0.63					
1 (n = 62)	36 (58)	15 (24)	5 (8)	6 (10)	< 0.05**
2 (n = 22)	12 (55)	8 (36)	2 (9)	0 (0)	
3 (n = 7)	4 (58)	1 (14)	1 (14)	1 (14)	

Note – *Mann-Whitney's U test. **Spearman's correlation coefficient by rank test. ***Procedures belonging to multi-groups are excluded from the analysis.

line drawn along the needle and a straight line drawn tangential to the pleura at the point of needle puncture. Pleural angle categories were divided into 3 groups: 0-50°(22/82 procedures: 27%), 51-70°(20/82 procedures: 24%) and > 70°(40/82 procedures: 49%), which excluded 9 procedures belonging to the multi-groups. Length of needle passes in the aerated lung was defined as calculation of total distance of the aerated lung traversed by the needle during each procedure (i.e. calculation of total distance of needle passes in one session). The length categories were divided into four groups: 0 mm (26 procedures: 28%), 1- 20 mm (37 lesions: 41%), 21-40 mm (21 procedures: 23%) and > 40mm (7 procedures: 8%). Number of harvesting sample categories were one (62 procedures: 68%), two (22 procedures: 24%) and three (7 procedures: 8%).

Clinical examination, postbiopsy CT, follow-up chest radiographs or CT and any management including air aspiration and chest tube placement were recorded during and after all procedures. The severity of pneumothorax during and after procedures was classified into four groups by the criteria of Ko, J.P. et al[8],: "none", "mild"; ≦1 cm "moderate"; 1-3 cm and "severe"; ≧ 3 cm, by lung surface retraction from the chest wall on postbiopsy CT and follow-up chest radiograph or CT. The largest lung surface retraction length between parallel lines to the parietal and visceral pleura was measured in the axial CT and chest radiograph of the whole lung and appropriated to the severity of pneumothorax. The largest length in the most severe status of pneumothorax during clinical examination was selected and used in the analysis.

The type and frequency of all complications, except pneumothorax, associated with the 91 procedures were also recorded during clinical examination.

Diagnostic yield was deemed a failure if adequate specimens could not be obtained to make a decision about benignity. Diagnostic accuracy, sensitivity and specificity were evaluated by comparing the results of biopsy and a confirmed diagnosis obtained by subsequent surgery or clinical follow-up course.

Statistical Analysis of Factors for Pneumothorax

Data analyses were performed with the use of computer software (Statcel2; OMS publishing, Tokorozawa, Japan). Univariate analysis was performed to evaluate the association between patient factors, lesion factors and procedure factors and the severity of pneumothorax. Two and multi groups in the categories of factors were analyzed using Mann-Whitney's U test and Spearman's correlation coefficient by rank test, respectively. The predominant risk factors for the severity of pneumothorax were determined by multivariate analyzing by multiple regression analysis of data derived from the univariate analysis. P values < 0.05 were defined as the statistical significant association in univariate and multivariate analysis.

RESULTS

The Severity of Pneumothorax

Pneumothorax occurred in 39/91 procedures (43%), which was revealed on postbiopsy CT in 36 procedures (40%) or subsequently by follow-up chest radiograph in 3 procedures (3%). Postbiopsy CT revealed the severity of pneumothorax as "none" for 55 procedures, "mild" for 26 procedures, "moderate" for 6 procedures and "severe" for 4 procedures. Air aspiration was performed for 3 out of 4 severe pneumothoraces on post biopsy CT. Two severe pneumothoraces were downgraded to moderate and one to no change. In the "none" group on postbiopsy CT, pneumothorax developed to "mild" in 1 procedure, "moderate" in 1 procedure and "severe" in 1 procedure on follow-up chest radiographs (= delayed pneumothorax). In the "mild" group on postbiopsy CT, 1 procedure developed to "moderate" and 2 procedures to "severe" on follow-up chest radiographs. The other pneumothoraces on postbiopsy CT remained stable or showed an improvement by follow-up in the classification of severity. A chest tube was placed one or two days after biopsy for "severe" in 3 (3%) of all procedures, which had developed from 1 procedure of "none" and 2 procedures of "mild", respectively.

Ultimately, the severity of pneumothorax in clinical examination for analysis resulted as "none" for 52 procedures (57%), "mild" for 24 procedures (26%), "moderate" for 8 procedures (9%) and "severe" for 7 procedures (8%).

Univariate analysis of factors for the severity of pneumothorax

Table 1-3 shows a summary of the results.

In patient factors (Table 1), there were no statistically significant associations between all factors and the severity of pneumothorax.

In lesion factors (Table 2), there were statistically significant associations between all factors and the severity of pneumothorax (lesion size, location and pleural contact; p-value < 0.05). Smaller size, lower location and non-pleural contact lesion presented a higher severity of pneumothorax.

In procedure factors (Table 3), there were statistically significant associations between number of pleural punctures, length of needle passes in the aerated lung and number of harvesting samples and the severity of pneumothorax (p-value < 0.05). Position, needle type, needle size, and pleural angle had no statistically significant associations with severity. The an increased number of pleural punctures, longer length of needle passes in the

aerated lung and increased number of harvesting samples presented a higher severity of pneumothorax.

Multivariate analysis of factors for the severity of pneumothorax

Table 4 shows a summary of the results.

Multiple regression analysis among statistical significant factors derived from univariate analysis showed that the factors of location, pleural contact, number of pleural punctures and number of harvesting samples had statistically significant association with the severity of pneumothorax (p-values < 0.05). Lesion size and length of needle passes in the aerated lung had no statistically significant associations with severity.

Other complications

Mild or moderate pulmonary hemorrhage on post biopsy CT or mild hemoptysis was seen in 41 procedures (45%) and mild hemothorax in 1 procedure (1%). All of these patients remained homodynamically stable and they were resolved conservatively. Fatal complications such as air embolism were not seen.

Diagnostic Yield and Accuracy of CT-guided biopsy

Ninety of 91 biopsy procedures (99%) yielded sufficient materials for cytological and/or histological analysis. One procedure contained only skeletal muscle tissues and was inadequate for diagnosis. The final diagnosis of 89 lung lesions, except for 2 lung lesions where sufficient material was not obtained and lost to follow up, was established as malignant in 65 (73 %) and benign in 24 (27%). Diagnostic sensitivity, specificity, and accuracy were 94% (65/69 procedures), 100% (20/20 procedures) and 96% (85/89 procedures), respectively.

DISCUSSION

In our study, the rate of pneumothorax was 43%, and that of requiring chest tube placement was 3%. There were no patients with severe hemorrhage. Diagnostic yield and accuracy were 99% and 96%, respectively. The results were acceptable compared to many reports[2-6, 8-11, 13-15]. Hence, our method of CT-guided lung biopsy is considered to be feasible.

Four factors, of location and pleural contact in lesion factors and number of pleural punctures and number of harvesting samples in procedure factors, were associated with the severity of pneumothorax by multiple regression analysis in our study.

Firstly, lower location as a risk factor is supported by the report of Saji, H. et al[10] that chest tube placement was required significantly. In our study, length of needle passes in the aerated lung in a lower location (mean length: 20.8 mm) was slightly longer than those in upper (mean length: 15.3 mm) and middle locations (mean length: 12.2 mm). Lung parenchyma might be more greatly damaged by needle passes in a lower location. In addition, the lower lung parenchyma moves more up and down to a greater degree. Needle motion during respiration could potentially widen the pleural puncture site and damage the lung parenchyma in the lower location.

Secondly, non-pleural contact lesion was a risk factor. The rates of pneumothorax in pleural contact and non-contact lesions were 30% and 67%, respectively. We consider that some pleural contact lesions seem to adhere to the pleura directly. The length of needle passes in the aerated lung in pleural contact lesions (mean: 9.6 mm) was apparently shorter than those in non-contact lesions (mean: 25.3 mm). Furthermore, 43% (25/58 procedures) of non-pleural contact lesions were biopsied without traversal of aerated lung. These are considered to lead to less damage to adjacent lung parenchyma. Cox, J.E. et al[2] reported that pleural-based lesions in which biopsy was performed without traversal of aerated lung, the pneumothorax rate was 15%. On the other hand, if any amount of aerated lung was traversed, it was 50%.

Table 4. Multivariate Analysis of Factors derived from Univariate Analysis

Factors	p value
Size	0.33
Location	0.019*
Pleural contact	0.035*
Number of pleural puncture	0.017*
Length of needle passes in the aerated lung	0.43
Number of harvesting samples	0.042*

Note – Data analysis is multiple regression analysis.
*There are statistically significant associations with the severity of pneumothorax (p value < 0.05).

Heck, S.L. et al[6] reported that the risk of severe pneumothorax was significantly higher if the lesion was completely surrounded by aerated lung (17% vs. 2%).

Lastly, increased numbers of pleural puncture and harvesting samples were risk factors. Mean numbers of pleural puncture and harvesting samples were 1.48 times and 1.40 times in all procedures. We withdrew the needle from the pleura in order to adjust its position in a very limited number of cases. We consider that the mechanisms as risk factors of these are almost equal. An increased number of pleural puncture sites clearly leads to greater lung parenchymal damage. When the visceral and parietal pleurae are no longer in contact, it is often difficult to pierce the visceral pleura with the biopsy needle[1]. In order to pierce the visceral pleura, a relatively swift needle puncture is needed. We performed additional pleural punctures (one time: 9 procedures, two times: 3 procedures and 3 times: 2 procedures) in 14 procedures under the presence of iatrogenic pneumothorax at the puncture site. The results of the severity of pneumothorax were "mild" in 7 procedures (50%) and "moderate" or "severe" in 7 procedures (50%). The rate of "moderate" and "severe" was higher than those of all pneumothoraces (15/39 procedures: 39%). We speculate that puncture of the visceral pleura induces enlarging of the pleural space with negative pressure and that air is drawn into the space. Saji, H. et al[10] proposed that the number of pleural puncture attempts should never exceed three.

The limitations of our study are its non-uniform method and its non-prospective native. Two different needle types were used for core and aspiration biopsy. There was a free choice of needle size ranging from 21 to 18-gauge, however, 20-gauge was most commonly used. Some reporters positively perform air aspiration for immediate, moderate or severe pneumothorax to avoid worsening pneumothorax[4, 12-15]. In our study, all three "severe" pneumothoraces on post biopsy CT led to immediate air aspiration and chest tube placement was not required. The criteria of Yamagami, T. et al[12, 13] for aspiration was involving more than seven slices with a width of 10 mm on postbiopsy CT. This almost corresponds to the "moderate" and "severe" grades in our definition. We consider that performing air aspiration for those grades of pneumothorax is desirable. In our study, all three cases that required chest tube placement either corresponded to delayed large pneumothoraces (1 procedure) or to enlarging pneumothoraces (2 procedures). Although we performed chest tube placement without late aspiration, aspiration may be useful for such pneumothoraces. Kazerooni, E.A. et al[7] reported that although pulmonary function test findings showed no correlation with the absolute frequency of pneumothorax, severity of obstructive pulmonary disease indicated by a reduced percentage of predicted forced expiratory volume in 1 second can be useful for identifying the patient population at high risk for requiring chest tube placement. However a pulmonary function test was not included in our protocol. Eventually, prospective trials by a uniform method, including biopsy technique and management for pneumothorax, will be desirable.

In conclusion, lower location, pleural contact, number of pleural punctures and number of harvesting samples were the predominant risk factors for the severity of pneumothorax after CT-guided percutaneous lung biopsy using the single-needle method. We consider that pleural punctures and number of harvesting samples should be kept to a minimum, in particular, for non-pleural contact lesions in a lower location, in order to avoid a higher severity of pneumothorax.

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Multimodality Bronchoscopic Diagnosis of Peripheral Lung Lesions

A Randomized Controlled Trial

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***Rationale*: Endobronchial ultrasound (EBUS) and electromagnetic navigation bronchoscopy (ENB) have increased the diagnostic yield of bronchoscopic diagnosis of peripheral lung lesions. However, the role of combining these modalities to overcome each individual technique's limitations and, consequently, to further increase the diagnostic yield remains untested.**

***Objectives*: A prospective randomized controlled trial involving three diagnostic arms: EBUS only, ENB only, and a combined procedure.**

***Methods*: All procedures were performed via flexible bronchoscopy and transbronchial forceps biopsies were obtained without fluoroscopic guidance. In the combined group, after electromagnetic navigation, the ultrasound probe was passed through an extended working channel to visualize the lesion. Biopsies were taken if ultrasound visualization showed that the extended working channel was within the target. Primary outcome was diagnostic yield. The reference "gold standard" was a surgical biopsy if bronchoscopic biopsy did not reveal a definite histological diagnosis compatible with the clinical presentation. Secondary outcomes were yields by size, lobar distribution, and lesion pathology. Complication rates were also documented.**

***Measurements and Main Results*: Of the 120 patients recruited, 118 had a definitive histological diagnosis and were included in the final analysis. The diagnostic yield of the combined procedure (88%) was greater than EBUS (69%) or ENB alone (59%; $p = 0.02$). The combined procedure's yield was independent of lesion size or lobar distribution. The pneumothorax rates ranged from 5 to 8%, with no significant differences between the groups.**

***Conclusions*: Combined EBUS and ENB improves the diagnostic yield of flexible bronchoscopy in peripheral lung lesions without compromising safety.**

Keywords: electromagnetic navigation bronchoscopy; ultrasound, interventional; solitary pulmonary nodule; transbronchial lung biopsy

Endobronchial ultrasound (EBUS) and electromagnetic navigation bronchoscopy (ENB) have increased the yield of flexible bronchoscopy in the diagnosis of peripheral lung lesions and solitary pulmonary nodules. The reported sensitivity of flexible bronchoscopy for the diagnosis of peripheral bronchogenic carcinoma ranges from 36 to 86% and is dependent on size (1, 2). Diagnostic yields for EBUS using a radial probe have been reported to be 58.3 to 80% (Table 1) (3–9), whereas ENB has reported yields of 69 to 74% (Table 2) (10–12). The yields of both these procedures are independent of lesion size (3–8, 12).

AT A GLANCE COMMENTARY

Scientific Knowledge on the Subject

Endobronchial ultrasound (EBUS) and electromagnetic navigation bronchoscopy (ENB) have increased the yield of flexible bronchoscopy in the diagnosis of peripheral lung lesions. Yet, direct comparisons and the role of combined diagnosis are unknown.

What This Study Adds to the Field

Combined EBUS and ENB improves the diagnostic yield of flexible bronchoscopy in peripheral lung lesions without compromising safety.

EBUS enables direct visualization of the target lesion before attempting biopsy. However, EBUS lacks a navigation system and requires the operator to maneuver the bronchoscope blindly to the lesion with the knowledge of prior radiological investigations like computed tomography (CT) scans. In previous studies, 11 to 24% of lesions could not be localized by EBUS (3, 5, 7, 9).

ENB consists of four components: an electromagnetic location board, a locatable sensor probe with an eight-way steering mechanism that is able to navigate the bronchial tree, an extending working channel (EWC) that can carry either the sensor probe or a flexible forceps, and computer software that converts CT scans into multiplanar images with three-dimensional virtual bronchoscopy reconstruction. This system enables real-time navigation guidance within the lungs to endobronchially invisible targets and subsequent biopsy through the EWC. However, biopsies using ENB have not always resulted in a diagnosis despite accurate navigation in the vast majority of cases to within 10 mm of the target center (10–12). Respiratory variations causing larger than anticipated navigation errors (10) and dislodgement of the EWC when biopsy instruments were introduced (12) may account for this lower than expected diagnostic yield. ENB lacks a means to directly visualize lesions before biopsy.

The role of combining EBUS with ENB to gain the benefits and minimize the limitations of either technique has never been reported. We performed a prospective randomized controlled trial comprising three arms with EBUS only, ENB only, and combined EBUS/ENB to test this hypothesis.

METHODS

We recruited 120 patients who were referred to the interventional pulmonology service at our centers between January 2003 and August 2006. Inclusion criteria were subjects above the age of 18, who signed informed consent and who were candidates for elective bronchoscopy or surgery. All subjects had evidence of peripheral lung lesions or

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TABLE 1. YIELD BY LESION SIZE IN STUDIES OF ENDOBRONCHIAL ULTRASOUND–GUIDED DIAGNOSIS OF PERIPHERAL LUNG LESIONS

Series	Technique	n	Size (*mm*)	Diagnostic Yield (%)
Herth and colleagues (3)	EBUS—transbronchial forceps biopsy	50	All	80
		21	< 30	80
		29	> 30	79
Kurimoto and colleagues (4)	EBUS with guide sheath and fluoroscopy ± curette—forceps biopsy/brush	150	All	77.3
		81	< 20	72.8
		43	20–30	77
		26	> 30	92
Kikuchi and colleagues (5)	EBUS with guide sheath and fluoroscopy ± curette—forceps biopsy/brush	24	< 30	58.3
		15	< 20	53.3
		9	20–30	66.7
Yang and colleagues (6)	EBUS—transbronchial forceps biopsy	122	All	65.6
		11	< 20	54.5
		103	> 20	66.0
Asahina and colleagues (7)	EBUS with guide sheath, virtual bronchoscopy navigation and fluoroscopy ± curette—forceps biopsy/brush	30	< 30	63.3
		18	< 20	44.4
		12	20–30	91.7
Paone and colleagues (8)	EBUS—transbronchial forceps biopsy	87	All	78.7
		25	< 20	71
		47	< 30	75
		40	> 30	82.8
Herth and colleagues (9)	EBUS—transbronchial forceps biopsy	54	Fluoroscopically invisible, mean 22 ± 0.7	70.3

Definition of abbreviation: EBUS = endobronchial ultrasound.

solitary pulmonary nodules on CT scans. Peripheral pulmonary lesions were defined as lesions that are surrounded by normal lung parenchyma without any CT evidence of endobronchial abnormalities. Pregnant patients and those with implantable pacemakers or defibrillators were excluded because of their untested nature in ENB. Randomization was achieved through a computer-generated random list. Both institutional review boards of the participating centers (Thoraxklinik and BIDMC) approved the data collection and analysis.

Primary outcome was diagnostic yield. If transbronchial lung biopsy failed to yield a definitive histological diagnosis that was consistent with the clinical presentation, then patients were referred for a surgical biopsy, which was considered the reference 'gold standard'. All patients with failed bronchoscopic diagnosis and who were unwilling or unable to have a surgical biopsy were excluded from final analysis to exclude possible confounders. Secondary outcomes included analysis of yield by lesion size, lobar location and lesion pathology (malignant versus benign). Safety of the procedures was documented by tracking all complications.

Bronchoscopy was performed in all three diagnostic arms of the study via the oral route using an Olympus IT160 adult therapeutic bronchoscope (Olympus, Tokyo, Japan) with a 2.8-mm working channel. Either moderate sedation or general anesthesia was used at the discretion of the operator. Patients who had general anesthesia were intubated before bronchoscopy. All cases were performed in an outpatient setting.

EBUS Procedure

A 20-MHz radial EBUS probe was used (UM-BS20–26R; Olympus, Tokyo, Japan). After inspection of the bronchial tree, the EBUS probe was inserted through a guide sheath/EWC (outer diameter, 2.0 mm; length, 850 mm) into the bronchi leading to the area where the lesion was suspected. Normal air-filled alveolar tissue typically produces a "snowstorm-like" whitish image. In contrast, solid lesions are darker and more homogeneous. When such images were seen, the probe was considered to be located within the target. The probe was then removed and biopsies were taken with regular disposable forceps. If the lesions were not identified by EBUS, then blind biopsies were taken from the suspected target area as per standard transbronchial biopsy.

ENB Procedure

The superDimension/Bronchus (superDimension, Inc., Plymouth, MN) system was used for ENB. All patients had noncontrast CT scans of the chest with slice thickness of 2 to 3.5 mm and slice interval (with overlap of 1 mm) of 1 to 2.5 mm. The initial planning phase involved importing the CT data into the superDimension software in DICOM (digital imaging and communications in medicine) format. Registration

TABLE 2. YIELD BY LESION SIZE IN STUDIES OF ELECTROMAGNETIC NAVIGATION–GUIDED DIAGNOSIS OF PERIPHERAL LUNG LESIONS

Series	Technique	n	Size (*mm*)	Diagnostic Yield (%)
Becker and colleagues (10)	ENB and fluoroscopy—forceps biopsy and brush	29	All	69
Schwarz and colleagues (11)	ENB and fluoroscopy—forceps biopsy and brush	13	All	69
		2	< 20	50
		11	> 20	73
Gildea and colleagues (12)	ENB and fluoroscopy—forceps biopsy and brush	54	All	74
		31	< 20	74.1
		23	> 20	73.9
		43	< 30	72.1
		11	> 30	81.8

Definition of abbreviation: ENB = electromagnetic navigation bronchoscopy.

points were marked by identifying five to seven prominent anatomic landmarks on the virtual bronchoscopy images. The center of the target lesion was also marked.

The patient was then placed on the electromagnetic location board (470 × 560 mm). Endobronchial mapping was achieved when the virtual fiducial registration points were linked to the actual position in the patient's thorax by a sensor probe (outer diameter, 1.9 mm). The software then documented the registration error, which represents the radius of the expected difference in location between the tip of the sensor probe in the actual patient and where the tip is expected to be. The registration error could then be reduced by either repositioning a misplaced landmark or by eliminating the landmarks with the greatest deviation. A registration error of 6 mm or less was considered acceptable.

After endobronchial inspection, navigation began by wedging the bronchoscope in the suspected bronchial segment and steering the sensor probe with the EWC to the lesion using the multiplanar CT images and the "tip-view" orientation. The EWC has a working length of 945 mm and requires a minimum bronchoscope instrument channel width of 2.0 mm. After navigation to the lesion was complete, specimens were obtained through the EWC by transbronchial forceps biopsy.

Combined EBUS/ENB

In the combined arm of our study, navigation to the lesion was first performed by ENB. When the lesion was located, the sensor probe was withdrawn and the EBUS probe was inserted through the EWC. If the EBUS image confirmed that the EWC was indeed within the target, we then proceeded on to forceps biopsy. However, if no acceptable EBUS image was obtained, renavigation with ENB and subsequent reconfirmation with EBUS was attempted before biopsies were taken.

Only forceps biopsies were taken in all three study arms and fluoroscopy was not used to guide transbronchial biopsies. Chest radiographs were taken after all procedures to exclude iatrogenic pneumothorax. Rapid onsite cytopathological evaluation was not used.

Data Analysis

Statistical analyses were performed using SAS statistical software (SAS Institute, Cary, NC). Continuous variables are expressed using mean, standard deviation, and range. Dichotomous variables are summarized as simple proportions. Baseline characteristics were analyzed using the Kruskal-Wallis test for continuous variables and the chi-square test for dichotomous variables. Overall yield and pneumothorax rates were analyzed with the chi-square or Fisher's exact test, as appropriate. Multivariate yield analysis by lesion size, lobar location, and disease type was done using the Cochran-Mantel-Haenszel test. A two-tailed p value of less than 0.05 indicated statistical significance.

RESULTS

Of the 120 recruited patients, 2 patients with a nondiagnostic bronchoscopic procedure declined surgical biopsy and were excluded from analysis. Both of these patients showed radiological stability in the size of lesion on clinical follow-up. Among the remaining 118 patients, 85 (72%) had a positive diagnostic result via bronchoscopy and the remaining 33 required a subsequent surgical biopsy to establish histological diagnosis. Although pulmonary function testing was not performed on all patients, these patients were all evaluated to be good surgical candidates by our thoracic surgeons.

Females accounted 42% of the 118 patients. The mean age was 53 ± 13 years, with a range of 19 to 81 years. No endobronchial lesions were seen in any of the patients. The overall prevalence of malignancy in our study was 78% (92/118). The mean number of biopsies taken was 4.1 ± 0.8, with a range of 2 to 5. There were no statistically significant differences among the three diagnostic arms of the study in terms of patient baseline characteristics, number of biopsies taken, type of sedation, lobar distribution of lesions, or pathology (i.e., malignant vs. benign) (Table 3). The final histological diagnoses are listed in Table 4 together with the respective bronchoscopic yields.

The mean lesion size was 26 ± 6 mm, with a range of 13 to 58 mm. The mean lesion size was larger in the group who underwent ENB only (28 ± 8 mm) compared with EBUS only (25 ± 5 mm) or combined EBUS/ENB (24 ± 5 mm; p = 0.01). However, there were no significant differences in size distribution across all three study arms when lesion size was classified as less than 20, 20 to 30, and more than 30 mm (p = 0.19).

Diagnostic Yield

Combined EBUS/ENB had a significantly higher diagnostic yield of 88% compared with EBUS (69%) or ENB alone (59%; p = 0.02). The enhanced yield of the combined procedure was also seen in analysis by lesion size, by lobar distribution, and for malignant pathology (Table 5). There was a trend toward improved

TABLE 3. BASELINE CHARACTERISTICS OF THE THREE DIAGNOSTIC ARMS

	EBUS n (%)	ENB n (%)	EBUS and ENB n (%)	p	Total n (%)
No. of patients	39	39	40		118
Female sex	16 (41)	19 (49)	15 (38)	0.59	50 (42)
Age, mean ± SD (range)	54 ± 12 (30–79)	55 ± 15 (19–81)	51 ± 12 (32–79)	0.42	53 ± 13 (19–81)
Type of sedation/anesthesia					
Moderate sedation	19 (49)	20 (51)	16 (40)	0.57	55 (47)
General anesthesia	20 (51)	19 (49)	24 (60)	0.57	64 (54)
No. of biopsies, mean ± SD (range)	4.1 ± 0.8 (3–5)	3.9 ± 0.9 (2–5)	4.2 ± 0.7 (3–5)	0.42	4.1 ± 0.8 (2–5)
Size in mm, mean ± SD (range)	25 ± 5 (17–35)	28 ± 8 (13–58)	24 ± 5 (14–32)	0.03*	26 ± 6 (13–58)
Distribution of lesion size					
⩽ 20 mm	9 (23)	4 (10)	10 (25)		23 (20)
20–30 mm	23 (59)	22 (56)	24 (60)	0.19	69 (58)
> 30 mm	7 (18)	13 (33)	6 (15)		26 (22)
Lobar location					
Right upper lobe	11 (28)	15 (39)	11 (28)		37 (31)
Right middle lobe	3 (8)	3 (8)	2 (5)		8 (7)
Right lower lobe	7 (18)	6 (15)	9 (23)	0.23	22 (19)
Left upper lobe	16 (41)	7 (18)	9 (23)		32 (27)
Left lower lobe	2 (5)	8 (21)	9 (23)		19 (16)
Benign lesions	7 (18)	10 (26)	9 (23)	0.71	26 (22)
Malignant lesions	32 (82)	29 (74)	31 (77)	0.71	92 (78)

Definition of abbreviations: EBUS = endobronchial ultrasound; ENB = electromagnetic navigation bronchoscopy.
* p < 0.05.

TABLE 4. DIAGNOSTIC YIELD BY HISTOLOGICAL DIAGNOSIS

Histological Diagnosis	n (%)	Yield (%)
Malignant lesions	92 (78)	73
Non–small cell carcinoma	79 (67)	73
Small cell carcinoma	3 (3)	100
Metastases	10 (9)	60
Benign lesions	26 (22)	69
Sarcoidosis	9 (8)	100
Tuberculosis	11 (9)	73
Harmatoma	4 (3)	0
Scar tissue	1 (1)	100
Cryptogenic organizing pneumonia	1 (1)	0
Total	118	72

sensitivity even in benign diseases, but because of the small sample size, this did not reach statistical significance. The diagnostic yield for all procedures performed under moderate sedation (67%) was not statistically different from procedures performed under general anesthesia (76%; $p = 0.28$).

EBUS and combined EBUS/ENB had diagnostic yields that were independent of lesion size and lobar distribution. Although the results of ENB alone were also independent of lesion size, the yields from the lower lobes were significantly lower (29%; $p = 0.01$).

Safety

The overall pneumothorax rate was 6% and there were no significant differences across the three study arms. (Table 5) All patients with post-procedure pneumothoraces were admitted for inpatient observation. Four cases were treated with chest drains: three with chest tubes and one with a small-bore catheter. One patient was managed with manual aspiration and observation. The two remaining cases required only observation and supplemental oxygen therapy. No cases of bleeding that required therapeutic interventions, such as ice saline instillation or endobronchial blocker placement, were recorded.

DISCUSSION

Multimodality investigation by combining EBUS with ENB enhances the diagnostic yield of flexible bronchoscopy in peripheral lung lesions compared with either procedure alone. The improved yield is unaffected by lesion size or lobar distribution. The 69% yield that was achieved in our EBUS-alone group was comparable to previous studies despite not using fluoroscopic guidance (3–9). Although our ENB-alone yield appears to be marginally lower (59 vs. 69–74%) compared with historical data, this may be attributable to factors other than fluoroscopy (10–12). In previous data, surgical biopsies were not always performed after nondiagnostic ENB procedures (12). Therefore, the definition of what constitutes a positive or negative yield is questionable. Furthermore, these studies used endobronchial brushes together with forceps, which could also have enhanced the yield (10–12).

The improved yield of the joint procedure is attributed to combining the ability of EBUS to directly visualize the internal structure of peripheral lung lesions with the precise navigation capabilities of ENB. As an adjunct to ENB, EBUS is superior to fluoroscopy in the detection of "fluoroscopically invisible" small lesions (9) and has the added advantage of being radiation free. Conversely, ENB enhances EBUS by providing real-time and subtle navigation through the steering mechanism of the locatable guide. This navigation capability is better than that afforded by either fluoroscopy (4, 5, 7) (yield, 58.3–77.3%), curettes (4, 5, 7) (yield, 58.3–77.3%), or virtual bronchoscopy (7) (yield, 63.3%). By guiding the EBUS probe to within the lesion rather than adjacent to it, yield is improved (4).

The strength of this study is that a gold-standard diagnosis was achieved in all analyzed patients when bronchoscopic results were inconclusive. This removed any ambiguity over how positive and negative yields were defined. By restricting biopsy technique to only forceps biopsy and not using other tools, such as needle, brush, and washings, possible confounders in yield and complications were eliminated. Although these biopsy techniques would be used in different combinations in usual clinical

TABLE 5. DIAGNOSTIC YIELDS BY SIZE, LOCATION, AND DISEASE TYPE, AND PNEUMOTHORAX RATE

	EBUS, n (%)		ENB, n (%)		EBUS and ENB, n (%)		p
Overall diagnostic yield	27/39 (69)		23/39 (59)		35/40 (88)		0.02*
Yield by lesion size							0.02*
⩽ 20 mm	7/9 (78)		3/4 (75)		9/10 (90)		
20–30 mm	16/23 (70)	p = 0.80	11/22 (50)	p = 0.50	21/24 (88)	p = 0.99	
> 30 mm	4/7 (57)		9/13 (69)		5/6 (83)		
Yield by lobar location							0.01*
Bilateral upper lobes	16/27 (59)		17/22 (77)		17/20 (85)		
Right middle lobe	3/3 (100)	p = 0.18	2/3 (67)	p = 0.01*	2/2 (100)	p = 0.99	
Bilateral lower lobes	8/9 (89)		4/11 (29)		16/18 (89)		
Yield for malignant disease							
Sensitivity	23/32 (72)		16/29 (55)		28/31 (90)		0.009*
Specificity	7/7 (100)		10/10 (100)		9/9 (100)		—
Positive predictive value	23/23 (100)		16/16 (100)		28/28 (100)		—
Negative predictive value	7/16 (44)		10/23 (44)		9/12 (75)		0.16
Yield for benign disease							
Sensitivity	4/7 (57)		7/10 (70)		7/9 (78)		0.79
Specificity	32/32 (100)		29/29 (100)		31/31 (100)		—
Positive predictive value	4/4 (100)		7/7 (100)		7/7 (100)		—
Negative predictive value	32/35 (91)		29/32 (91)		31/33 (94)		0.90
Pneumothorax rate	2/39 (5)		2/39 (5)		3/40 (8)		0.99

For definition of abbreviations, *see* Table 3.
* $p < 0.05$.

practice, varying biopsy instruments, number of passes, volume of lavage (injected and aspirated), and specimen handling might have introduced too many variables into our study.

Although there was a statistically significant difference in the size of the lesions in the ENB-alone arm of this study, the 3- to 4-mm difference in mean size may be clinically irrelevant. Furthermore, there was no difference in the distribution of lesion size across the three arms. Our results also confirm data collected from previous studies that yields of both EBUS and ENB are independent of size (3–8, 12). Hence, lesion size is unlikely to confound our findings.

The greatly diminished lower lobe yield of 29% in the ENB-alone arm could be attributed to navigation error. Navigation in the lower lobes may be more affected by diaphragmatic movement during breathing. This is because the planning data are based on CT images acquired in a single breath hold and cannot compensate for respiratory movements (10).

There was also no increase in pneumothorax rate by combining EBUS with ENB. The pneumothorax rate in either EBUS (5%) or ENB (5%) was not greatly increased compared with that reported in previous studies (0–4.2%) (5, 7, 12). Fluoroscopy was not used in this study because earlier data have shown that it does not decrease the rate of iatrogenic pneumothorax after transbronchial lung biopsy using regular flexible bronchoscopy (13, 14). Moreover, previous studies on EBUS-guided diagnosis of peripheral lung lesions did not use fluoroscopy because the target lesions were small and would have been difficult to visualize on fluoroscopy (9). The other disadvantages of fluoroscopy are radiation exposure and space constraints in the bronchoscopy suite. Furthermore, the 8% pneumothorax rate of combined ENB/EBUS compares favorably with the 23 to 38% pneumothorax rate reported in CT-guided transthoracic biopsy (15, 16).

Significant endobronchial bleeding was also not encountered. The EWC, which enables multiple biopsy samples to be taken from the same area after navigation, also facilitates tamponade of potential bleeding by allowing the scope to remain wedged at the subsegmental bronchi throughout the biopsy process (5, 7).

There are possible concerns that, in combined EBUS/ENB, the procedure duration may be extended. Although procedure duration was not studied in this trial, no adverse events related to sedation or anesthesia were documented. Previous data comparing EBUS-directed biopsy with fluoroscopically directed biopsy show only a marginal increase in biopsy time (9.8 vs. 8.1 min) (8). In ENB, the average reported registration times are 2 to 3 minutes and navigation times are about 7 minutes (10, 12). There may also be some time saved in ENB if C-arm fluoroscopy is not used. Therefore, the combined EBUS/ENB procedure is likely to require additional time, but this may only be a marginal increase.

Before embarking on advanced diagnostic bronchoscopy, issues of costs and training need to be addressed. A detailed cost-analysis model is beyond the scope of this study. At the time this manuscript was prepared, the EBUS EU-M30S-K processor cost $31,000 and the UM-BS20–26R-3 radial probes cost $6,250. This probe can be used for approximately 50 cases. The superDimension/Bronchus system for ENB costs $129,450 and the disposable sensor probes together with the EWC cost $995. Reimbursement issues for ENB have also not been clarified. The recommended training requirement for EBUS is at least 50 proctored procedures (17). No guidelines are currently available for ENB.

Multimodality diagnosis with the joint use of EBUS with ENB has pushed the diagnostic yield of flexible bronchoscopic procedures closer to the sensitivity obtainable through either transthoracic CT-guided (92%) (1) or surgical ($\sim$ 100%) (18) biopsies. The proven comfort (19) and safety (20) of flexible bronchoscopy and the recognized risks of these other procedures (15, 16, 18, 21, 22) establishes multimodality bronchoscopy with combined EBUS/ENB as a viable alternative. Radiation exposure to the patient and operating staff is also eliminated by not using fluoroscopy. By using other biopsy techniques, such as transbronchial needles and brushes, the diagnostic yield is likely to be further enhanced (1, 23). The ultimate goal of reliable and minimally invasive biopsy of peripheral lung lesions now appears feasible.

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The Effect of Cup Versus Alligator Forceps on the Results of Transbronchial Lung Biopsy

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Background: Transbronchial lung biopsy (TBLB) is a routine diagnostic procedure for pulmonary diseases and is performed by using either the alligator or cup forceps. The purpose of this study was to compare the role of the type of forceps in the quality and complications of TBLB.

Methods: This was a prospective, observational, double-blinded study. Four samples were taken from each patient through TBLB. Characteristics of the samples, including sample size and number of alveoli, whether it was diagnostic or not, and side effects such as pneumothorax and bleeding, were all recorded.

Results: One hundred seventy-six biopsy samples obtained from 44 patients were evaluated; 21 patients (47.7%) were male. Of the 88 samples taken with an alligator forceps, based on size, 21.6% were small, 45.5% were medium, and 33% were large. Corresponding results for the samples taken with a cup forceps were 43.2% small, 29.5% medium, and 27.3% large. Of the 88 biopsy samples taken with an alligator forceps, 18.2% were diagnostic; this rate was 23.9% for cup forceps. Significant pneumothorax was not seen in any of the cases in the alligator forceps group, but it was detected in 9% of the cases in the cup forceps group. Significant bleeding was seen in 1% of the alligator forceps and 5.7% of the cup forceps procedures.

Conclusions: Our study results, comparing the effect of 2 different kinds of forceps on TBLB results, were consistent with those of other studies with larger samples ($P = 0.008$) using alligator forceps. The diagnostic value of the procedures was not significantly different ($P = 0.355$).

Key Words: transbronchial lung biopsy, cup forceps, alligator forceps

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Lung biopsy through the bronchus [transbronchial lung biopsy (TBLB)] is a commonly used diagnostic procedure and is used to diagnose a variety of pulmonary conditions, such as interstitial lung disease (sarcoidosis), vascular disease (vasculitis), small airway disease (obstructive bronchiolitis), malignant conditions (alveolar cell carcinoma), and opportunistic infections.[1]

This procedure was first performed by using a flexible bronchoscope in 1974.[2]

TBLB is mainly performed using 2 different kinds of forceps: alligator and cup forceps. There have been several studies on the diagnostic sensitivity of TBLB but the results have not been consistent.[2]

TBLB is associated with complications such as bleeding and pneumothorax.[3] Complication rate may vary with the use of different forceps. Thus, it is important to evaluate biopsy samples taken with different types of forceps in terms of their diagnostic utility.

Some studies have evaluated the quality of samples based on sample size and content of alveoli.[4,5] Yet, major characteristics have not been described determining the quality of the biopsy samples.[6]

Our study was aimed at comparing the effect of the type of forceps used based on diagnostic utility and safety of samples obtained with TBLB.

METHODS

This was a prospective, double-blind, observational study conducted in the interventional pulmonology ward of Masih Daneshvari Hospital, a referral center for pulmonary diseases in Tehran, Iran, and was approved by the institutional review board and ethics committee of the hospital. Patients who were scheduled to undergo bronchoscopy and TBLB for infiltrative processes seen in the chest x-ray were considered for the study. Patients who had a history of significant bleeding during an earlier bronchoscopy or a blood coagulation abnormality were excluded from the study. On the basis of a reference from earlier studies, our sample size was calculated to be 40 patients in each type of forceps group. All patients signed written informed consent to participate in the trial. Patients were consecutively enrolled and alternatively assigned to the use of either alligator or cup forceps.

Local anesthesia was induced using 2 mL of 5% lidocaine spray through the nose. No sedation was required during the procedure and fluoroscopy was not used. Two types of forceps were used to obtain proper samples. The alligator forceps was Alligator

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Jaw Type FB-15C-1 (Olympus) and the cup forceps was Standard Type Fenestrated FB-19C-1 (Olympus), and both were reusable. The patients, the pathologist, and the assistant were all blinded to the type of forceps used.

During a video-assisted bronchoscopy procedure, 4 biopsy samples were obtained from areas with the most radiographic abnormalities.

Sample size was described by the assistant as follows:

If the sample did not fill the forceps, it would be considered as a small size sample; if it filled the forceps, it would be considered medium; and if it was larger than the forceps size, it would be considered a large sample.

At the end of the procedure, complications such as pneumothorax or bleeding were also assessed. If the bleeding was not significant and did not require any intervention, it was considered "mild." If suctioning was required to clear the bronchoscopy field, the bleeding was considered "moderate," and if interventions such as the use of ice-cold saline, topical adrenaline, or balloon tamponade were required, it was considered "significant."

A chest x-ray was obtained after each bronchoscopic procedure.

If pneumothorax did not take place, the case was assigned as "no pneumothorax." If the size of pneumothorax was closer than 2.5 cm to the chest wall on chest x-ray, it was graded as "mild," and it was graded as "significant" if it was further than 2.5 cm from the chest wall or required a chest tube placement.

Subsequently, the samples were sent for histopathologic examination. From each biopsy, at least 24 tissue sections were prepared (4 slides) and the number of alveoli in each sample was counted and classified by the pathologist as follows:

1. Alveoli greater than 20: Alveolated
2. Alveoli < 20: Nonalveolated
3. No alveoli: Unsatisfactory

All the samples were evaluated by 1 pathologist in a blinded manner and are described as follows:

1. The studied tissue yielded a pathological diagnosis: Diagnostic
2. The studied tissue did not yield a pathological diagnosis: Nondiagnostic

The prominent tissue present in each sample was described by the pathologist as parenchyma, bronchial mucosa, surface epithelium, pleura, necrotic tissue, or lacking pulmonary tissue.

RESULTS

Forty-four patients were recruited in the study, of which 21 (47.7%) were male. Among the 21 male patients, 11 underwent biopsy using alligator forceps and 10 using cup forceps. Among the 23 female patients, 11 underwent biopsy using alligator forceps and 12 using cup forceps.

The youngest patient was 16 years old and the oldest was 71 years (3 individuals). The mean age of the patients was 46.6 years.

A total of 176 biopsy samples were collected from 44 patients (4 each).

Sample Grouping Based on Size

Of a total of 176 samples, 57 were small (32.4%), 66 were medium (37.5%), and 53 were large (30.1%) (Table 1).

Sample Distribution Based on the Type of Forceps

Of the 88 samples taken by the alligator forceps, 19 were small (21.6%), 40 were medium (45.5%), and 29 were large (33.0%).

Of the 88 samples obtained by the cup forceps, 38 were small (43.2%), 26 were medium (29.5%), and 24 were large (27.3%).

The number of small samples taken by the cup forceps ($n = 38$) was twice the number of those taken by the alligator forceps ($n = 19$). This difference was smaller regarding medium and large samples. The type of forceps used was significantly correlated with the sample size ($P = 0.008$). In other words, with the alligator forceps larger samples were taken as compared with the cup forceps.

Alveolation of Samples

Of a total of 176 samples, 84 were alveolated (47.7%), 26 were nonalveolated (14.8%), and 66 were unsatisfactory (37.5%) (Table 2).

Grouping Based on the Type of Forceps

Of a total of 88 samples taken by the alligator forceps, 42 were alveolated (47.7%), 18 were nonalveolated (20.5%), and 28 were unsatisfactory (31.8%); whereas, of a total of 88 samples obtained by the cup forceps, 42 samples were alveolated

TABLE 1. Results of Sample Size

	Forceps		
	Alligator	Cup	Total
Small			
N	19	38	57
% within forceps	21.6%	43.2%	32.4%
Medium			
N	40	26	66
% within forceps	45.5%	29.5%	37.5%
Large			
N	29	24	53
% within forceps	33.0%	27.3%	30.1%
Total			
N	88	88	176
% within forceps	100.0%	100.0%	100.0%

N indicates number.

TABLE 2. Number of Alveoli

	Forceps		
Number of Alveoli	Alligator	Cup	Total
>20			
N	42	42	84
% within forceps	47.7%	47.7%	47.7%
<20			
N	18	8	26
% within forceps	20.5%	9.1%	14.8%
No alveoli			
N	28	38	66
% within forceps	31.8%	43.2%	37.5%
Total			
N	88	88	176
% within forceps	100.0%	100.0%	100.0%

N indicates number.

(47.4%), 8 were nonalveolated (9.1%), and 38 were unsatisfactory (43.2%).

The number of samples with more than 20 alveoli was similar for the 2 types of forceps used. However, the number of samples without alveoli was higher in the cup forceps group (38 samples vs. 28 samples), but this difference was not statistically significant ($P = 0.065$).

Diagnostic Value

Of a total of 176 samples, 38 were diagnostic (21%) (Tables 3, 4).

On the basis of the type of forceps used, of the 88 samples taken by the alligator forceps, 16 were diagnostic (18.2%), whereas of the 88 samples obtained by the cup forceps, 21 were diagnostic (23.9%).

The number of diagnostic samples obtained with the cup forceps was more than that of the alligator forceps (21 samples vs. 16 samples), but the difference was not statistically significant ($P = 0.355$).

Pneumothorax

Of a total of 44 patients, 41 showed no pneumothorax (93.2%), 1 patient (4 samples) showed mild pneumothorax (2.3%), and significant pneumothorax was present in 2 cases (8 samples) that required chest tube placement (4.5%).

TABLE 3: Final Diagnosis

	Frequency	Percent
Granulomatous disease	10	26.3
Constrictive bronchiolitis	2	5.3
Malignant process	9	23.7
Lymphoproliferative disorder	3	7.9
Organizing pneumonia	4	10.5
Eosinophilic pneumonitis	2	5.3
Hypersensitivity pneumonitis	1	2.6
Pneumocystis infection	3	7.9
Vasculitis	1	2.6
Alveolar hemorrhage	1	2.6
Lymphocytic interstitial pneumonitis	2	5.3
Total	38	100.0

TABLE 4. Final Diagnosis and Type of Forceps Used

	Forceps		
	Alligator	Cup	Total
Diagnostic			
N	9	12	21
% within forceps	40.9%	54.5%	47.7%
Nondiagnostic			
N	13	10	23
% within forceps	59.1%	45.5%	52.3%
Total			
N	22	22	44

N indicates number.

As noted earlier, mild pneumothorax occurred in 1 case, which resolved with needle aspiration.

The frequency of pneumothorax based on the type of forceps used was as follows:

Of a total of 22 patients in the alligator forceps group, 21 patents showed no pneumothorax (95.5%), 1 patient showed mild pneumothorax (4.5%), and significant pneumothorax was not found in any patient (0%).

Of a total of 22 patients in the cup forceps group, 20 patients had no pneumothorax (90.9%), mild pneumothorax was not found (0%), and 2 patients developed significant pneumothorax (9.1%).

According to the above-mentioned results, no significant association was found between the type of forceps used and the development of pneumothorax ($P = 0.999$).

Bleeding

The frequency of bleeding was as follows: 114 biopsies were not associated with any bleeding (64.8%), 56 had mild bleeding (31.8%), and 6 caused significant bleeding (3.4%); even in cases with significant hemorrhage, bleeding easily stopped with ice-cold saline or adrenaline instillation. No uncontrollable bleeding occurred (Table 5).

Bleeding frequency based on the type of forceps used was as follows:

Of a total of 88 samples taken by the alligator forceps, 59 had no bleeding (67%), 28 had mild bleeding (31.8%), and 1 had significant bleeding (1.1%). Of a total of 88 samples obtained by the cup forceps, 55 had no bleeding (62.5%), 28 had mild bleeding (31.8%), and 5 had significant bleeding (5.7%).

According to the above findings, only in the latter situation (significant bleeding) was the number of cases in the cup forceps group comparatively larger than that of the alligator forceps group (5 vs. 1); however, this difference was not statistically significant ($P = 0.246$).

TABLE 5. Severity of Bleeding

	Forceps		
	Alligator	Cup	Total
No bleeding			
N	59	55	114
% within forceps	67.0%	62.5%	64.8%
Mild			
N	28	28	56
% within forceps	31.8%	31.8%	31.8%
Significant			
N	1	5	6
% within forceps	1.1%	5.7%	3.4%
Total			
N	88	88	176
% within forceps	100.0%	100.0%	100.0%

N indicates number.

DISCUSSION

In a study by Curley et al,[7] the effect of factors such as different types of forceps, size, flotation, and number of samples on quality and diagnostic value of sampling was studied, and it was concluded that the diagnostic value of the sample is increased by the following measures: (a) size of forceps, (b) number of samples per biopsy, and (c) type of forceps (alligator forceps).

Visher and Faro[8] in their study emphasized the diagnostic role of TBLB in pediatric illnesses and concluded that the use of adult-sized bronchoscopes with larger working channels, instead of pediatric bronchoscopes, can increase the diagnostic sensitivity of bronchoscopy.

In a study on the diagnostic ability of biopsy of peripheral pulmonary lesions, alligator forceps yielded more sensitivity as compared with standard forceps.[9]

In this study, a significant correlation was found between the biopsy sample size and type of forceps used, and larger samples were obtained by alligator forceps (21.6% small specimens with alligator vs. 43.2% with cup forceps).[7] Therefore, it was concluded that alligator forceps provide larger biopsy samples.

In our study, from a total of 176 specimens, 37 (21%) were diagnostic. In comparison with the other studies, we do not feel that the size of our samples, number of alveolated samples, or the diagnostic yield was any different.[7–9] Among the 88 specimens taken by each of the 2 different kinds of forceps, 18 samples (18.2%) in the alligator forceps group and 21 samples (23.9%) in the cup forceps group were diagnostic; however, this difference was not statistically significant. Maybe with a larger study sample size a statistically significant result can be obtained. In similar studies, even though no significant difference was found between the 2 types of forceps in terms of abnormal or alveolated tissue, the cup forceps provided a smaller specimen with less diagnostic value. In this study, although the alligator forceps yielded larger samples, the diagnostic yield was not increased. The relatively low diagnostic yield is most likely related to the case mix of various suspected diagnoses.

Although in 6 specimens (3.4%) bleeding was moderate to severe, requiring lavage with ice-cold saline and/or local adrenaline, uncontrollable bleeding was not found in any of the cases and significant bleeding (requiring more than 10 mL of normal saline for irrigation) was observed in 5 cases in the cup forceps group and in 1 case in the alligator forceps group. However, this difference was not statistically significant, which may be because of a small sample size. A larger study sample may yield more conclusive results.

In general, 3 individuals had pneumothorax, which was resolved in 1 case with needle aspiration and in 2 cases required chest tube placement. The first case was in the alligator forceps group and the latter 2 were in the cup forceps group. In other words, pneumothorax was more frequent in the cup forceps group, but it was not statistically significant. Similar studies have not shown any cases of pneumothorax. Development of pneumothorax in 3 cases in our study may have been because of the lack of fluoroscopic guidance.

According to our study results, the incidence of postprocedure bleeding and pneumothorax was higher in those who underwent biopsy with the cup forceps.

It is noteworthy that 12.3% of the cases with small biopsy samples developed pneumothorax, whereas this rate was much lower in cases with medium or large biopsy samples. In other words, contrary to our expectation, obtaining a larger size of biopsy specimen is not necessarily associated with more complications.

In conclusion, the alligator forceps yield a larger specimen than did cup forceps.

No significant difference was seen in the diagnostic yield between the 2 types of forceps. Biopsy complications (pneumothorax and bleeding) occur less frequently when using alligator forceps, but the difference in this regard is not statistically significant. Larger studies are indicated.

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assessment of diagnostic utility. *Chest*. 1992;102: 748–752.
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7. Curley FJ, Johal JS, Burke ME, et al. Transbronchial lung biopsy: can specimen quality be predicted at the time of biopsy? *Chest*. 1998;113:1037–1041.
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ATTACHMENT 3

(b) (4) **Clinical Evaluation Report for the superTrax® Triple Needle-Tipped Cytology Brush**

1. PURPOSE

This Clinical Evaluation Report details the Clinical safety of the superTrax® Triple Needle-Tipped Cytology Brush. Because cytology brushes have been clinically used for a long period of time and no significant new technology is being introduced, a literature review approach is deemed acceptable to evaluate the clinical safety and effectiveness of the superTrax Triple Needle-tipped Cytology brush products. This clinical evaluation Report is intended to assess risks compared to the benefits associated with the use of the products.

2. SCOPE

This document is intended to show conformity with the Essential Requirements of the European Council Directive 93/42/EEC and the Global Harmonization Task force summary technical documentation to demonstrate clinical safety and efficacy. This document will review the risk analyses, literature, complaints and competitive products to evaluate the potential clinical risks associated with Triple Needle-Tipped cytology brushes.

Currently there are two models of the Triple Needle-Tipped Cytology brush designated as shown below.

Order Number	Part Name
SDTNB1000	10 mm superTrax Triple Needle Tipped Brush
SDTNB1500	15 mm superTrax Triple Needle Tipped Brush

3. APPLICABLE DOCUMENTS AND QUALITY RECORDS

(b) (4) Clinical Evaluation Plan for the superTrax® Triple Needle-Tipped Cytology Brush

4. PROCEDURE

(b) (4)

5. CONCLUSION

The Clinical evaluation concluded that the level of risk associated with the superDimension Cytology Brush is acceptable and that the benefits outweigh the risks. Therefore, the devices in their intended use should not include any additional risks to patient safety not previously identified in the risk analysis. No additional clinical data is required.

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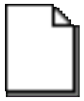
2. Tochigi, N., S. Dacic, and N.P. Ohori, *Bronchoscopic and transthoracic cytology and biopsy for pulmonary nonsmall cell carcinomas: performance characteristics by procedure and tumor type.* Diagn Cytopathol. **40**(8): p. 659-63.
3. Michels, G., et al., *Usefulness of imprint and brushing cytology in diagnosis of lung diseases with flexible bronchoscopy.* J Clin Pathol. **65**(7): p. 649-53.
4. Dobler, C.C. and A.B. Crawford, *Bronchoscopic diagnosis of endoscopically visible lung malignancies: should cytologic examinations be performed routinely?* Intern Med J, 2009.
5. Rhee, C.K., et al., *Diagnostic yield of flexible bronchoscopy without fluoroscopic guidance in evaluating peripheral lung lesions.* J Bronchology Interv Pulmonol. **17**(4): p. 317-22.
6. Roth, K., et al., *Predictors of diagnostic yield in bronchoscopy: a retrospective cohort study comparing different combinations of sampling techniques.* BMC Pulm Med, 2008. **8**: p. 2.
7. Griffin, J.P., et al., *Diagnosis of lung cancer: a bronchoscopist's perspective.* J Bronchology Interv Pulmonol. **19**(1): p. 12-8.
8. Asano, F., et al., *Deaths and complications associated with respiratory endoscopy: a survey by the Japan Society for Respiratory Endoscopy in 2010.* Respirology. **17**(3): p. 478-85.
9. Carr, I.M., et al., *Blood loss during flexible bronchoscopy: a prospective observational study.* Respiration. **84**(4): p. 312-8.

Attachments

APPENDIX A: Instructions for Use Documents for the superDimension Triple Needle Cytology Brushes



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APPENDIX B: Articles Evaluated for Clinical Relevance and Level of Evidence

No.	Reference	Specific Device	Intended Use	Level of Evidence	Relevant Outcome Measures	Appropriate Follow-up	Statistical Significance	Clinical Significance	Total Grade	Included in Literature Review
			1= Same use 2=Minor deviation 3=Major deviation	1=Randomized Controlled Trial 2=Nonrandomized Controlled Trial 3=Observational Study with Controls 4=Observational Study without Controls	1=Yes 2=No	1=Yes 2=No	1=Yes 2=No	1=Yes 2=No		
1.	**Author** Michels, Guido 1; Topalidis, Theodoros 2; Buttner, Reinhard 3; Engels, Marianne 3; Pfister, Roman 1 **Title** Usefulness of imprint and brushing cytology in diagnosis of lung diseases with flexible bronchoscopy.[Article] **Source** Journal of Clinical Pathology. 65(7):649-653, July 2012.	N.S.	1	3	1	1	2	1	9	Yes
2.	**Author** Griffin, John P. MD *; Zaman, Muhammad K. MD *; Niell, Harvey B. MD +; Tolley, Elizabeth A. PhD ++; Cole, F. Hammond Jr MD [S]; Weiman, Darryl S. MD, JD [//] **Title** Diagnosis of Lung Cancer: A Bronchoscopist's Perspective.[Article] **Source** Journal of Bronchology & Interventional Pulmonology. 19(1):12-18, January 2012.	.								
3.	**Author** Tochigi, Naobumi M.D., Ph.D. 1; Dacic, Sanja M.D., Ph.D. 1; Ohori, Paul N. M.D. 1* **Title** Bronchoscopic and Transthoracic Cytology and Biopsy for Pulmonary Nonsmall Cell Carcinomas: Performance Characteristics by Procedure and Tumor Type.[Article] **Source** Diagnostic Cytopathology. 40(8):659-663, August 2012.	N.S.	1	3	1	1	1	1	8	Yes
4.	**Author** Sigel, Carlie S. MD *; Moreira, Andre L. MD, PhD *; Travis, William D. MD *; Zakowski, Maureen F. MD *; Thornton, Raymond H. MD +; Riely, Gregory J. MD, PhD ++; Rekhtman, Natasha MD, PhD * **Title** Subtyping of Non-small Cell Lung Carcinoma: A Comparison of Small Biopsy and Cytology Specimens.[Article] **Source** Journal of Thoracic Oncology. 6(11):1849-1856, November 2011.	N.S.	1	3	2	1	2	1	10	No

5.	**Author** Tatar D. Gunes E. Erbaycu A.E. Yucel N. Halilcolar H. **Title** The contribution of bronchoalveolar lavage performed before and after bronchoscopic biopsies to the diagnosis of peripheral lung cancer. **Source** UHOD - Uluslararasi Hematoloji-Onkoloji Dergisi. 21 (2) (pp 80-86), 2011. Date of Publication: 2011.	N.S.	1	2	2	1	2	1	9	No
6.	**Author** Dobler, C. C.; Crawford, A. B. H. **Title** Bronchoscopic diagnosis of endoscopically visible lung malignancies: should cytological examinations be carried out routinely?.[Article] **Source** Internal Medicine Journal. 39(12):806-811, December 2009.	N.S.	1	3	1	1	1	1	8	Yes
7.	**Author** Roth K. Hardie J.A. Andreassen A.H. Leh F. Lind Eagan T.M. **Title** Cost minimization analysis for combinations of sampling techniques in bronchoscopy of endobronchial lesions. **Source** Respiratory Medicine. 103 (6) (pp 888-894), 2009. Date of Publication: June 2009.	N.S	1	2	2	1	1	2	9	No
8.	**Author** Rhee, Chin Kook MD; Kang, Hyun Hui MD; Kang, Ji Young MD; Kim, Jin Woo MD, PhD; Kim, Yong Hyun MD; Park, Shin Ae MD; Moon, Hwa Sik MD, PhD; Lee, Sang Haak MD, PhD **Title** Diagnostic Yield of Flexible Bronchoscopy Without Fluoroscopic Guidance in Evaluating Peripheral Lung Lesions.[Article] **Source** Journal of Bronchology & Interventional Pulmonology. 17(4):317-322, October 2010.	N.S.	1	4	1	1	1	1	9	Yes
9.	**Author** Roth K, Eagan TM, Andreassen AH, Leh F, Hardie JA **Title** A randomised trial of endobronchial ultrasound guided sampling in peripheral lung lesions. **Source** Lung cancer (Amsterdam, Netherlands). 74(2):219-25, 2011 Nov.	Boston Scientific Celebrity	1	1	2	1	2	2	9	No
10.	**Author** Roth K. Hardie J.A. Andreassen A.H. Leh F. Eagan T.M. **Title** Predictors of diagnostic yield in bronchoscopy: a retrospective cohort study comparing different combinations of sampling techniques. **Source** BMC pulmonary medicine. 8 (pp 2), 2008. Date of Publication: 2008.	Boston Scientific Celebrity	1	3	1	1	1	1	8	Yes

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		Revision	(b) (4)
Document Title:	Clinical Evaluation Report for the superTrax® Triple Needle-Tipped Cytology Brush	Effective	
Owner:	(b) (4), (b) (6)		

11.	**Author** ASANO, FUMIHIRO 1; AOE, MOTOI 1; OHSAKI, YOSHINOBU 1; OKADA, YOSHINORI 1; SASADA, SHINJI 1; SATO, SHIGEKI 1; SUZUKI, EIICHI 1; SENBA, HIROSHI 1; FUJINO, SHOZO 1; OHMORI, KAZUMITSU 1 **Title** Deaths and complications associated with respiratory endoscopy: A survey by the Japan Society for Respiratory Endoscopy in 2010.[Article] **Source** Respirology. 17(3):478-485, April 2012.	N.S.	1	4	1	1	2	2	11	Yes
12.	**Author** Carr, Ighsaan M. a; Koegelenberg, Coenraad F.N. a; von Groote-Bidlingmaier, Florian a; Mowlana, Abdurasiet a; Silos, Kim a; Haverman, Thijs a; Diacon, Andreas H. a, b; Bolliger, Chris T. a **Title** Blood Loss during Flexible Bronchoscopy: A Prospective Observational Study.[Miscellaneous Article] **Source** Respiration. 84(4):312-318, September 2012.	N.S.	1	4	1	1	1	2	10	Yes
13.	**Author** Ishida, Takashi 1; Asano, Fumihiro 2; Yamazaki, Koichi 3; Shinagawa, Naofumi 3; Oizumi, Satoshi 3; Moriya, Hiroshi 4; Munakata, Mitsuru 1; Nishimura, Masaharu 3; for the Virtual Navigation in Japan (V-NINJA) trial group **Title** Virtual bronchoscopic navigation combined with endobronchial ultrasound to diagnose small peripheral pulmonary lesions: a randomised trial.[Article] **Source** Thorax. 66(12):1072-1077, December 2011.	N.S.	1	1	2	2	2	2	10	No
14.	**Author** Pang, B. 1,2; Matthias, D. 3; Ong, C. W. 1; Dhewar, A. N. 2; Gupta, S. 2; Lim, G. L. 2; Nga, M. E. 2; Seet, J. E. 2; Qasim, A. 2; Chin, T. M. 1,4; Soo, R. 1,4; Soong, R. 1,2; Salto-Tellez, M. 1,5 **Title** The positive impact of cytological specimens for EGFR mutation testing in non-small cell lung cancer: a single South East Asian laboratory's analysis of 670 cases.[Article] **Source** Cytopathology. 23(4):229-236, August 2012.	N.S.	1	3	2	1	1	1	9	No

15.	**Author** Choudhury M. Singh S. Agarwal S. **Title** Efficacy of bronchial brush cytology and bronchial washings in diagnosis of non neoplastic and neoplastic bronchopulmonary lesions. **Source** Turk Patoloji Dergisi/Turkish Journal of Pathology. 28 (2) (pp 142-146), 2012. Date of Publication: 2012.	N.S.	1	2	1	1	2	1	8	Yes

APPENDIX C: Articles resulting from the Search Criteria that are out of scope for this Clinical Evaluation

Number	Reference	Reason for Exclusion
1.	**Author** Bian J-J, Wang J-F, Wan X-J, Zhu K-M, Deng X-M **Title** [Preparation of a fiberoptic bronchoscopy training box and evaluation of its efficacy] LA: Chi **Source** Academic Journal of Second Military Medical University. 31(1):80-3, 2010.	Foreign Language (n=1)
2.	**Author** Durra, Heba MD; Flieder, Douglas B. MD + **Title** Peripheral Squamous Cell Carcinoma of the Lung: Potential Pitfalls in Biopsy Interpretation.[Review] **Source** Pathology Case Reviews. 17(5):211-216, September/October 2012.	Case Reports (n=18)
3.	**Author** Schwarz, C. a; Bittner, R. b; Kirsch, A. e; Loddenkemper, C. d; Mairinger, T. c; Schonfeld, N. a; Serke, M. a; Loddenkemper, R. f **Title** A 62-Year-Old Woman with Bilateral Pleural Effusions and Pulmonary Infiltrates Caused by Extramedullary Hematopoiesis.[Article] **Source** Respiration. 78(1):110-113, 2009.	
4.	**Author** Ozsu S. Erol M.M. Oztuna F. Ersoz S. Kavgaci H. Aksoy H.Z. **Title** Endobronchial metastasis from testicular seminoma. **Source** Medical Principles and Practice. 17 (6) (pp 493-495), 2008. Date of Publication: October 2008.	
5.	**Author** Modrykamien, Ariel MD 1*; Arrossi, Andrea MD 2; Reddy, Anita MD 1 **Title** A 50-year-old man with stage 2 sarcoidosis with pleural involvement.[Report] **Source** Journal Of Hospital Medicine. 4(4):E1-E3, April 2009.	
6.	**Author** Zhang, X. [Author]; Xu, L. [Author]; Wang, L. L. [Author]; Liu, S. [Author]; Li, J. [Author]; Wang, X. [Author, Reprint Author; E-mail: cm4hwxgn2005@126.com]. **Title** Bronchopulmonary Infection with Lophomonas blattarum: a Case Report and Literature Review **Source** Journal of International Medical Research. 39(3). MAY-JUN 2011. 944-949.	
7.	**Author** Reagan, Jennifer K. DVM; Aronsohn, Michael G. VMD, DACVS **Title** Acute onset of dyspnea associated with Oslerus osleri infection in a dog.[Report] **Source** Journal of Veterinary Emergency and Critical Care. 22(2):267-272, April 2012.	
8.	**Author** Guozhong Y. **Title** Bronchopulmonary infection with lophomonas blattarum: Two cases report and literature review. **Source** Journal of Medical Colleges of PLA. 23 (3) (pp 176-182), 2008. Date of Publication: 2008.	
9.	**Author** Desai, Ashesh D. MD * +; Bandi, Venkata MD +; Holzhauser, Luise MD +; Loebe, Matthias MD ++; Noon, George MD ++; Lunn, William MD + **Title** Bleeding After Biopsy of a Bronchial Artery Arteriovenous Malformation Presenting as an Endobronchial Mass: Case Report and Literature Review.[Report] **Source** Journal of Bronchology. 15(3):176-178, July 2008.	
10.	**Author** Venkatram, Sindhaghatta MD, FCCP *; Ogugua, Chukwuma MD *; Niazi, Masooma MD +; Diaz-Fuentes, Gilda MD, FCCP ++ **Title** Pulmonary Pleomorphic Carcinoma Mimicking Bronchopneumonia in an Elderly Man.[Report] **Source** Journal of Bronchology & Interventional Pulmonology. 16(1):55-58, January 2009.	
11.	**Author** Liu, Wei M.D. 1; Palma-Diaz, Fernando M.D. 2; Alasio, Teresa M. M.D. 1* **Title** Primary Small Cell Carcinoma of the Lung Initially Presenting as a Breast Mass: A Fine-Needle Aspiration Diagnosis.[Article] **Source** Diagnostic Cytopathology. 37(3):208-212, March 2009.	
12.	**Author** Bilaceroglu, Semra MD, FCCP *; Gursoy, Soner MD +; Yucel, Nur MD ++; Ozbilek, Engin MD [S] **Title** Inflammatory Myofibroblastic Tumor Presenting as a Large Mass and a Spontaneously Resolving Nodule in the Lung.[Report] **Source** Journal of Bronchology & Interventional Pulmonology. 16(4):286-289, October 2009.	
13.	**Author** Usuda, Katsuo MD, FCCP; Sagawa, Motoyasu MD; Aikawa, Hirokazu MD; Tanaka, Makoto MD; Machida, Yuichiro MD; Ueno, Masakatsu MD; Sakuma, Tsutomu MD **Title** Virtual Bronchoscopic Navigation is Useful in the Diagnosis of Synchronous Pulmonary Squamous Cell Carcinomas: Report of a Case.[Report] **Source** Journal of Bronchology. 15(2):104-106, April 2008.	
14.	**Author** McIntire, Maria M.D. 1; Shah, Neha D. M.D. 2; Kim, Anthony W. M.D. 3; Gattuso, Paolo M.D. 1*; Liptay, Michael J. M.D. 3 **Title** Cytologic Imprints of Giant Atypical Bronchopulmonary Carcinoid Tumor of the Lung With Extensive Oncocytic Component.[Article] **Source** Diagnostic Cytopathology. 36(12):887-890, December 2008.	
15.	**Author** Luh, Shi-ping 1; Kuo, Chih 2; Tsao, Thomas Chang-yao 3 **Title** Breast metastasis from small cell lung carcinoma.[Report] **Source** Journal of Zhejiang University SCIENCE B. 9(1):39-43, January 2008.	
16.	**Author** Abul Y. Eryuksel E. Celikel C. Tosuner Z. Yazici Z. Karakurt S. **Title** Endobronchial metastasis of malignant melanoma presenting with dyspnea: Case report and literature review. **Source** Turkiye Klinikleri Journal of Medical Sciences. 31 (2) (pp 468-470), 2011. Date of Publication: 2011.	
17.	**Author** Reyes C.V. Jensen J.D. **Title** Transbronchial fine-needle aspiration cytology. **Source** Community Oncology. 7 (11) (pp 511-513), 2010. Date of Publication: November 2010.	

18.	**Author** Shelton, David A. M.B.Ch.B. 1*; Rana, Durgesh N. M.B.B.S., M.D., F.R.C.Path. 1; Holbrook, Miles B.M.B.S., B.Med.Sci., F.R.C.Path. 1; Taylor, Paul M.B.Ch.B., F.R.C.R., F.R.C.P. 1; Bailey, Simon M.B.Ch.B., M.R.C.P. 1 **Title** Adenosquamous carcinoma of the lung diagnosed by cytology?: A diagnostic dilemma.[Report] **Source** Diagnostic Cytopathology. 40(9):830-833, September 2012.	
19.	**Author** Morency, Elizabeth M.D. 1; Rodriguez Urrego, Paula A. M.D. 1; Szporn, Arnold H. M.D. 1; Beth Beasley, Mary M.D. 1; Chen, Hua M.D., Ph.D. 1,* **Title** The "drunken honeycomb" feature of pulmonary mucinous adenocarcinoma: A diagnostic pitfall of bronchial brushing cytology.[Report] **Source** Diagnostic Cytopathology. 41(1):63-66, January 2013.	
20.	**Author** Lommatzsch, Steven E.; Martin, Richard J.; Good, James T. Jr **Title** Importance of fiberoptic bronchoscopy in identifying asthma phenotypes to direct personalized therapy.[Miscellaneous Article] **Source** Current Opinion in Pulmonary Medicine. 19(1):42-48, January 2013.	Device not Evaluated (n=123)
21.	**Author** Goyal, Shilpa M.D. 1,*; Mohan, Harsh M.D., M.N.A., M.S., F.I.C.Path. 1; Uma Handa, M.D. 1; Saini, Varinder M.D. 2 **Title** Rinse fluid and imprint smear cytology of bronchial biopsies in diagnosis of lung tumors.[Article] **Source** Diagnostic Cytopathology. 40(2):98-103, February 2012.	
22.	**Author** Liu Y.-Z. Jiang Y.-Y. Hao J.-J. Lu S.-S. Zhang T.-T. Shang L. Cao J. Song X. Wang B.-S. Cai Y. Zhan Q.-M. Wang M.-R. **Title** Prognostic significance of MCM7 expression in the bronchial brushings of patients with non-small cell lung cancer (NSCLC). **Source** Lung Cancer. 77 (1) (pp 176-182), 2012. Date of Publication: July 2012.	
23.	**Author** Evison M. Munavvar M. **Title** Flexible bronchoscopy. **Source** Medicine. 40 (4) (pp 190-193), 2012. Date of Publication: April 2012.	
24.	**Author** Aikawa, Emiko CT 1; Kawahara, Akihiko PhD 1,*,+; Hattori, Satoshi PhD 2; Yamaguchi, Tomohiko CT 1; Abe, Hideyuki CT 1; Taira, Tomoki CT 1; Azuma, Koichi MD, PhD 3; Kage, Masayoshi MD, PhD 1 **Title** Comparison of the expression levels of napsin A, thyroid transcription factor-1, and p63 in nonsmall cell lung cancer using cytocentrifuged bronchial brushings.[Article] **Source** Cancer Cytopathology. 119(5):335-345, October 25, 2011.	
25.	**Author** Schramm, Martin MD 1; Wrobel, Christian 1; Born, Ingmar 1; Kazimirek, Marietta 1; Pomjanski, Natalia MD 1; William, Marina MD 2; Kappes, Rainer MD 3; Gerharz, Claus Dieter MD, PhD 4; Biesterfeld, Stefan MD, PhD 1,*; Bocking, Alfred MD, PhD 1 **Title** Equivocal cytology in lung cancer diagnosis:Improvement of diagnostic accuracy using adjuvant multicolor FISH, DNA-image cytometry, and quantitative promoter hypermethylation analysis.[Article] **Source** Cancer Cytopathology. 119(3):177-192, June 25, 2011.	
26.	**Author** Kobayashi, Yukihiro [Author, Reprint Author]; Uehara, Takeshi [Author]; Ota, Hiroyoshi [Author]. **Title** Liquid-Based Thin-Layer Cytology Can Be Routinely Used in Samples Obtained via Fiberoptic Bronchoscope **Source** Acta Cytologica. 55(1). 2011. 69-78.	
27.	**Author** Dragan A.-M. Rosca E. Mutiu G. **Title** Cytologic and histopathologic diagnosis in bronchopulmonary squamous cell carcinoma. **Source** Romanian Journal of Morphology and Embryology. 52 (SUPPL. 1) (pp 395-398), 2011. Date of Publication: 2011.	
28.	**Author** Lang T.U. Khalbuss W.E. Monaco S.E. Pantanowitz L. **Title** Solitary tracheobronchial papilloma: Cytomorphology and ancillary studies with histologic correlation. **Source** CytoJournal. 8 , 2011. Article Number: 6. Date of Publication: 2011.	
29.	**Author** Chambers D.C. Hodge S. Hodge G. Yerkovich S.T. Kermeen F.D. Reynolds P. Holmes M. Hopkins P.M.A. **Title** A novel approach to the assessment of lymphocytic bronchiolitis after lung transplantationtransbronchial brush. **Source** Journal of Heart and Lung Transplantation. 30 (5) (pp 544-551), 2011. Date of Publication: May 2011.	
30.	**Author** Hirst, Robert A. PhD; Rutman, Andrew; Williams, Gwyneth HND; O'Callaghan, Chris MD, PhD **Title** Ciliated Air-Liquid Cultures as an Aid to Diagnostic Testing of Primary Ciliary Dyskinesia.[Article] **Source** Chest. 138(6):1441-1447, December 2010.	
31.	**Author** Domagala-Kulawik J. Gornicka B. Krenke R. Mich S. Chazan R. **Title** The value of cytological diagnosis of small cell lung carcinoma. **Source** Pneumonologia i alergologia polska : organ Polskiego Towarzystwa Ftyzjopneumonologicznego, Polskiego Towarzystwa Alergologicznego, i Instytutu Gruzlicy i Chorob Pluc. 78 (3) (pp 203-210), 2010. Date of Publication: 2010.	
32.	**Author** Dooms C. Seijo L. Gasparini S. Trisolini R. Ninane V. Tournoy K.G. **Title** Diagnostic bronchoscopy: State of the art. **Source** European Respiratory Review. 19 (117) (pp 229-236), 2010. Date of Publication: September 1, 2010.	
33.	**Author** Kim, Stacey MD 1; Owens, Christopher L. MD 1* **Title** Analysis of ThinPrep cytology in establishing the diagnosis of small cell carcinoma of lung.[Article] **Source** Cancer Cytopathology. 117(1):51-56, February 25, 2009.	
34.	**Author** Gilad, Shlomit [Author]; Lithwick-Yanai, Gila [Author]; Barshack, Iris [Author]; Benjamin, Sima [Author]; Krivitsky, Irit [Author]; Edmonston, Tina Bocker [Author]; Bibbo, Marluce [Author]; Thurm, Craig [Author]; Horowitz, Laurie [Author]; Huang, Yajue [Author]; Feinmesser, Meora [Author]; Hou, J. Steve [Author]; St Cyr, Brianna [Author]; Burnstein, Ilanit [Author]; Gibori, Hadas [Author]; Dromi, Nir [Author]; Sanden, Mats [Author]; Kushnir, Michal [Author]; Aharonov, Ranit [Author, Reprint Author; E-mail: ranit_ah@rosettagenomics.com]. **Title** Classification of the Four Main Types of Lung Cancer Using a MicroRNA-Based Diagnostic Assay **Source** Journal of Molecular Diagnostics. 14(5). SEP 2012. 510-517.	
35.	**Author** Good, James T. Jr MD, FCCP; Kolakowski, Christena A. MS; Groshong, Steve D. MD, PhD; Murphy, James R. PhD; Martin, Richard J. MD, FCCP **Title** Refractory Asthma: Importance of Bronchoscopy to Identify Phenotypes and Direct Therapy.[Article] **Source** Chest. 141(3):599-606, March 2012.	

36.	**Author** Shah, Archan MBBS *; Ost, David MD; Jimenez, Carlos MD; Morice, Rodolfo MD; Yarmus, Lonny MD; Filner, Joshua MD; Eapen, George MD **Title** Complications Related to Endobronchial Ultrasound Guided Transbronchial Needle Aspiration. On behalf of the ACCP Quality Improvement Registry Education and Evaluation (AQuIRE) Participants*.[Miscellaneous] **Source** Chest. 140(4_MeetingAbstracts) (Supplement 4):865A, October 2011.	
37.	**Author** Fujita, Yoshitsugu 1,*; Seki, Nobuhiko 1; Kurimoto, Noriaki 2; Inoue, Ken 3; Miyazawa, Teruomi 4; Abe, Tadashi 5; Eguchi, Kenji 1 **Title** Introduction of Endobronchial Ultrasonography (EBUS) in Bronchoscopy Clearly Reduces Fluoroscopy Time: Comparison of 147 Cases in Groups Before and After EBUS Introduction.[Article] **Source** Japanese Journal of Clinical Oncology. 41(10):1177-1181, October 2011.	
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111.	**Author** Hamad, Laila Omar [Author, Reprint Author; E-mail: lailahamadi@yahoo.com]; Vervoorts, Anja [Author]; Hennig, Thomas [Author]; Bayer, Rainer [Author]. **Title** Ex vivo photodynamic diagnosis to detect malignant cells in oral brush biopsies **Source** Lasers in Medical Science. 25(2). MAR 2010. 293-301.	
112.	**Author** Bruno, Andreina PhD a; Pace, Elisabetta MD a; Chanez, Pascal MD b; Gras, Delphine PhD b; Vachier, Isabelle PhD c; Chiappara, Giuseppina PhD a; La Guardia, Maurizio MD d; Gerbino, Stefania PhD a,d; Profita, Mirella PhD a; Gjomarkaj, Mark MD a **Title** Leptin and leptin receptor expression in asthma.[Miscellaneous Article] **Source** Journal of Allergy & Clinical Immunology. 124(2):230-237e4, August 2009.	
113.	**Author** Yahaya, B. [Author, Reprint Author; E-mail: badrul@kck.usm.my]; Baker, A. [Author]; Tennant, P. [Author]; Smith, S. H. [Author]; Shaw, D. J. [Author]; McLachlan, G. [Author]; Collie, D. D. S. [Author]. **Title** Analysis of airway epithelial regeneration and repair following endobronchial brush biopsy in sheep **Source** Experimental Lung Research. 37(9). NOV 2011. 519-535.	
114.	**Author** Athanasiadis, Theo MBBS; Beule, Achim G. MD; Robinson, Brian H. PhD; Robinson, Simon R. FRACS; Shi, Z Bsc, GDip Science, MSc; Wormald, Peter-John MD **Title** Effects of a Novel Chitosan Gel on Mucosal Wound Healing Following Endoscopic Sinus Surgery in a Sheep Model of Chronic Rhinosinusitis.[Miscellaneous Article] **Source** Laryngoscope. 118(6):1088-1094, June 2008.	
115.	**Author** Konge, Lars MD; Arendrup, Henrik MD; von Buchwald, Christian DMSc; Ringsted, Charlotte PhD **Title** Virtual Reality Simulation of Basic Pulmonary Procedures.[Article] **Source** Journal of Bronchology & Interventional Pulmonology. 18(1):38-41, January 2011.	
116.	**Author** Griesenbach, U 1,4,5; McLachlan, G 2,4,5; Owaki, T 3; Somerton, L 1,4; Shu, T 3; Baker, A 2,4; Tennant, P 2,4; Gordon, C 2,4; Vrettou, C 2,4; Baker, E 2,4; Collie, D DS 2,4; Hasegawa, M 3; Alton, E WFW 1,4 **Title** Validation of recombinant Sendai virus in a non-natural host model.[Article] **Source** Gene Therapy. 18(2):182-188, February 2011.	
117.	**Author** Rogers, Geraint B. 1; Carroll, Mary P. 2; Bruce, Kenneth D. 1 **Title** Studying bacterial infections through culture-independent approaches.[Review] **Source** Journal of Medical Microbiology. 58(11):1401-1418, November 2009.	
118.	**Author** Yang, Youwen PhD; Haitchi, Hans Michael MD; Cakebread, Julie PhD; Sammut, David MD; Harvey, Anna BSc; Powell, Robert M. PhD; Holloway, John W. PhD; Howarth, Peter MD, PhD; Holgate, Stephen T. MD, DSc; Davies, Donna E. PhD **Title** Epigenetic mechanisms silence a disintegrin and metalloprotease 33 expression in bronchial epithelial cells.[Article] **Source** Journal of Allergy & Clinical Immunology. 121(6):1393-1399e14, June 2008.	
119.	**Author** Dougherty, Ryan H. MD a,b,c; Sidhu, Sukhvinder S. PhD a; Raman, Kavita PhD d; Solon, Margaret BA a,b; Solberg, Owen D. PhD a,b; Caughey, George H. MD a,b,d; Woodruff, Prescott G. MD, MPH a,b; Fahy, John V. MD, MSc a,b **Title** Accumulation of intraepithelial mast cells with a unique protease phenotype in TH2-high asthma.[Miscellaneous Article] **Source** Journal of Allergy & Clinical Immunology. 125(5):1046-1053e8, May 2010.	
120.	**Author** Thomas, Titus MRCP 1; Kaye, Phillip V. FRCPath 2; Ragunath, Krish MD, DNB, MPhil, MRCP 1; Aithal, Guruprasad MD, PhD, FRCP 1 **Title** Efficacy, Safety, and Predictive Factors for a Positive Yield of EUS-Guided Trucut Biopsy: A Large Tertiary Referral Center Experience.[Article] **Source** American Journal of Gastroenterology. 104(3):584-591, March 2009.	
121.	**Author** HUANG, Chun-Ta 1; HO, Chao-Chi 2,3; TSAI, Yi-Ju 4; YU, Chong-Jen 2; YANG, Pan-Chyr 2 **Title** Factors influencing visibility and diagnostic yield of transbronchial biopsy using endobronchial ultrasound in peripheral pulmonary lesions.[Article] **Source** Respirology. 14(6):859-864, August 2009.	

122.	**Author** Travis, William D. MD; Brambilla, Elisabeth MD; Noguchi, Masayuki MD; Nicholson, Andrew G. MD; Geisinger, Kim R. MD; Yatabe, Yasushi MD; Beer, David G. PhD; Powell, Charles A. MD; Riely, Gregory J. MD; Van Schil, Paul E. MD; Garg, Kavita MD; Austin, John H. M. MD; Asamura, Hisao MD; Rusch, Valerie W. MD; Hirsch, Fred R. MD; Scagliotti, Giorgio MD; Mitsudomi, Tetsuya MD; Huber, Rudolf M. MD; Ishikawa, Yuichi MD; Jett, James MD; Sanchez-Cespedes, Montserrat PhD; Sculier, Jean-Paul MD; Takahashi, Takashi MD; Tsuboi, Masahiro MD; Vansteenkiste, Johan MD; Wistuba, Ignacio MD; Yang, Pan-Chyr MD; Aberle, Denise MD; Brambilla, Christian MD; Flieder, Douglas MD; Franklin, Wilbur MD; Gazdar, Adi MD; Gould, Michael MD, MS; Hasleton, Philip MD; Henderson, Douglas MD; Johnson, Bruce MD; Johnson, David MD; Kerr, Keith MD; Kuriyama, Keiko MD; Lee, Jin Soo MD; Miller, Vincent A. MD; Petersen, Iver MD, PhD; Roggli, Victor MD; Rosell, Rafael MD; Saijo, Nagahiro MD; Thunnissen, Erik MD; Tsao, Ming MD; Yankelewitz, David MD **Title** International Association for the Study of Lung Cancer/American Thoracic Society/European Respiratory Society International Multidisciplinary Classification of Lung Adenocarcinoma.[Review] **Source** Journal of Thoracic Oncology. 6(2):244-285, February 2011.
123.	**Author** Yarmus, Lonny DO, FCCP *; Van der Kloot, Thomas MD +; Lechtzin, Noah MD *; Napier, Mark MD +; Dressel, Douglas MD +; Feller-Kopman, David MD, FCCP * **Title** A Randomized Prospective Trial of the Utility of Rapid On-Site Evaluation of Transbronchial Needle Aspirate Specimens.[Article] **Source** Journal of Bronchology & Interventional Pulmonology. 18(2):121-127, April 2011.
124.	**Author** Linden, Philip A. MD **Title** Use of Navigation Bronchoscopy for Biopsy and Endobronchial Fiducial Placement.[Miscellaneous Article] **Source** Innovations: Technology & Techniques in Cardiothoracic & Vascular Surgery. 6(4):271-275, July/August 2011.
125.	**Author** Colt, Henri G +,2; Davoudi, Mohsen 1; Murgu, Septimiu 1 **Title** Scientific evidence and principles for the use of endobronchial ultrasound and transbronchial needle aspiration.[Review] **Source** Expert Review of Medical Devices. 8(4):493-513, July 2011.
126.	**Author** Zamani, Adil **Title** Bronchoscopic intratumoral injection of tranexamic acid: a new technique for control of biopsy-induced bleeding.[Report] **Source** Blood Coagulation & Fibrinolysis. 22(5):440-442, July 2011.
127.	**Author** Mukhopadhyay, Sanjay 1; Farver, Carol F 2; Vaszar, Laszlo T 3; Dempsey, Owen J 4; Popper, Helmut H 5; Mani, Haresh 6; Capelozzi, Vera L 7; Fukuoka, Junya 8; Kerr, Keith M 9; Zeren, E Handan 10,11; Iyer, Venkateswaran K 12; Tanaka, Tomonori 8; Narde, Ivy 7; Nomikos, Angheliki 9; Gumurdulu, Derya 10; Arava, Sudheer 12; Zander, Dani S 6; Tazelaar, Henry D 13 **Title** Causes of pulmonary granulomas: a retrospective study of 500 cases from seven countries.[Article] **Source** Journal of Clinical Pathology. 65(1):51-57, January 2012.
128.	**Author** Oki, Masahide MD, PhD *; Saka, Hideo MD *; Kitagawa, Chiyoe MD, PhD *; Kogure, Yoshihito MD *; Murata, Naohiko MD *; Adachi, Takashi MD *; Ando, Masahiko MD, PhD + **Title** Randomized Study of Endobronchial Ultrasound-Guided Transbronchial Biopsy: Thin Bronchoscopic Method versus Guide Sheath Method.[Article] **Source** Journal of Thoracic Oncology. 7(3):535-541, March 2012.
129.	**Author** Fielding, D. I. 1; Chia, C. 1; Nguyen, P. 1; Bashirzadeh, F. 1; Hundloe, J. 1; Brown, I. G. 1; Steinke, K. 2 **Title** Prospective randomised trial of endobronchial ultrasound-guide sheath versus computed tomography-guided percutaneous core biopsies for peripheral lung lesions.[Article] **Source** Internal Medicine Journal. 42(8):894-900, August 2012.
130.	**Author** Huang, Chun-Ta C.-T. a, b; Tsai, Yi-Ju Y.-J. c; Liao, Wei-Yu W.-Y. a; Wu, Pei-Chen P.-C. d; Ho, Chao-Chi C.-C. a; Yu, Chong-Jen C.-J. a; Yang, Pan-Chyr P.-C. a **Title** Endobronchial Ultrasound-Guided Transbronchial Biopsy of Peripheral Pulmonary Lesions: How Many Specimens Are Necessary?.[Miscellaneous] **Source** Respiration. 84(2):128-134, August 2012.
131.	**Author** Wang Memoli, Jessica S MD; Nietert, Paul J. PhD; Silvestri, Gerard A. MD, FCCP **Title** Meta-analysis of Guided Bronchoscopy for the Evaluation of the Pulmonary Nodule.[Article] **Source** Chest. 142(2):385-393, August 2012.
132.	**Author** Wang, Ying-Ting MS a; Han, Yi-Ping MD b,*; Li, Qiang MD b; Chen, He-Zhong MD c **Title** Recurrence of sarcoidosis: The follow-up of splenic involvement.[Article] **Source** Heart & Lung: Journal of Acute & Critical Care. 41(6):e44-e48, November 2012.
133.	**Author** Zulqarnain, Sikander MD *; Pesola, Gene R. MD, MPH *; Borczuk, Alain C. MD +; Moche, Jason A. MD ++ **Title** Primary Ciliary Dyskinesia With Central Pair Agenesis: A Rare Cause of Adult Bronchiectasis.[Miscellaneous Article] **Source** Clinical Pulmonary Medicine. 19(6):243-245, November 2012.
134.	**Author** Kokkonouzis, Ioannis 1,2; Strimpakos, Alexios S. 1; Lampaditis, Ioannis 2; Tsimpoukis, Sotirios 1; Syrigos, Kostas N. 1,* **Title** The Role of Endobronchial Ultrasound in Lung Cancer Diagnosis and Staging: A Comprehensive Review.[Review] **Source** Clinical Lung Cancer. 13(6):408-415, November 2012.
135.	**Author** TAY, JUN H. 1; IRVING, LOUIS 1,5; ANTIPPA, PHILLIP 2,6; STEINFORT, DANIEL P. 1,3,4 **Title** Radial probe endobronchial ultrasound: Factors influencing visualization yield of peripheral pulmonary lesions.[Article] **Source** Respirology. 18(1):185-190, January 2013.
136.	**Author** Weiser, Todd S. MD *; Hyman, Kevin MD; Yun, Jaime MD; Litle, Virginia MD; Chin, Cythinia MD; Swanson, Scott J. MD **Title** Electromagnetic Navigational Bronchoscopy: A Surgeon's Perspective.[Miscellaneous Article] **Source** Annals of Thoracic Surgery,The. 85(2):S797-S801, February 2008.

137.	**Author** Baumann, Hans Joerg MD a; Kluge, Stefan MD a; Balke, Lorenz MD a; Yekebas, Emre MD a; Izbicki, Jakob R. MD a; Amthor, Michael MD b; Kreymann, Georg MD a; Meyer, Andreas MD a **Title** Yield and safety of bedside open lung biopsy in mechanically ventilated patients with acute lung injury or acute respiratory distress syndrome.[Report] **Source** Surgery. 143(3):426-433, March 2008.	
138.	**Author** Herth, Felix J.F. a; Morgan, Ross K. MD b; Eberhardt, Ralf MD a; Ernst, Armin MD, FCCP a,b,* **Title** Endobronchial Ultrasound-Guided Miniforceps Biopsy in the Biopsy of Subcarinal Masses in Patients with Low Likelihood of Non-Small Cell Lung Cancer.[Article] **Source** Annals of Thoracic Surgery,The. 85(6):1874-1878, June 2008.	
139.	**Author** Koh, M. S. 1; Tee, A. 1; Wong, P. 1; Antippa, P. 2; Irving, L. B. 1 **Title** Advances in lung cancer diagnosis and staging: endobronchial ultrasound.[Article] **Source** Internal Medicine Journal. 38(2):85-89, February 2008.	
140.	**Author** Hur, Jin MD *; Lee, Hye-Jeong MD *; Byun, Min Kwang MD +; Nam, Ji Eun MD *; Moon, Jin Wook MD +; Kim, Hua Sun MD *; Kim, Young Jin MD *; Choe, Kyu Ok MD *; Choi, Byoung Wook MD, PhD *++ **Title** Computed Tomographic Fluoroscopy-Guided Needle Aspiration Biopsy as a Second Biopsy Technique After Indeterminate Transbronchial Biopsy Results for Pulmonary Lesions: Comparison With Second Transbronchial Biopsy.[Miscellaneous Article] **Source** Journal of Computer Assisted Tomography. 34(2):290-295, March/April 2010.	
141.	**Author** Pearlstein, Daryl Phillip MD a,c,*; Quinn, Curtis C. MD c,d; Burtis, Charles C. BS a; Ahn, Kwang Woo PhD b; Katch, Aaron J. MS b **Title** Electromagnetic Navigation Bronchoscopy Performed by Thoracic Surgeons: One Center's Early Success.[Article] **Source** Annals of Thoracic Surgery,The. 93(3):944-950, March 2012.	
142.	**Author** Berntsen R. Nielsen EW. **Title** Bronchoscopy in rural areas?. **Source** Pulmonary Medicine. 2012:872327, 2012.	
143.	**Author** Mehta, Pankaj MD *; Trikha, Girish MD **Title** Lymphoproliferative Disorder of the Lung.[Report] **Source** Chest. 140(4_MeetingAbstracts) (Supplement 4):69A, October 2011.	Abstract Only (n=5)
144.	**Author** Shahzad, Saleem MD *; Suryanarayanan, Manoj MD; Nallagatla, Sasikanth MD; Verma, Vishal MD; Vasudevan, Viswanath MD; Arjomand, Farhad MD; Ali, Rana MD; Reminick, Scott MD **Title** A 70-Year-Old Woman With Endobronchial Fibroepithelial Polyp.[Report] **Source** Chest. 140(4_MeetingAbstracts) (Supplement 4):45A, October 2011.	
145.	**Author** Bessich, Jamie MD *; Munson, Jeffrey MD **Title** A Primary Pulmonary Carcinoma With Combined Neuroendocrine and Squamous Cell Features in a Patient With Long-standing Tripe Palms and Digital Clubbing.[Report] **Source** Chest. 140(4_MeetingAbstracts) (Supplement 4):30A, October 2011.	
146.	**Author** Yim, Eric MD *; Weiman, Darryl MD **Title** A Case of Lung Herniation Into Postpneumonectomy Space.[Report] **Source** Chest. 140(4_MeetingAbstracts) (Supplement 4):28A, October 2011.	
147.	**Author** Tiernan, J F; Wallace, W; Skwarski, K M **Title** S40 Early experience of endobronchial ultrasound-miniprobe (EBUS-MP) for investigation of peripheral pulmonary mass lesions.[Miscellaneous] **Source** Thorax. 65(Suppl_4) (Supplement 1):A20-A21, December 2010.	
148.	**Author** Hallstrand T.S. Wurfel M.M. Lai Y. Ni Z. Gelb M.H. Altemeier W.A. Beyer R.P. Aitken M.L. Henderson W.R. **Title** Transglutaminase 2, a novel regulator of eicosanoid production in asthma revealed by genome-wide expression profiling of distinct asthma phenotypes. **Source** PloS one. 5 (1) (pp e8583), 2010. Date of Publication: 2010.	Duplicate References (n=11)
149.	**Author** Lang TU. Khalbuss WE. Monaco SE. Pantanowitz L. **Title** Solitary Tracheobronchial Papilloma: Cytomorphology and ancillary studies with histologic correlation. **Source** Cytojournal. 8:6, 2011.	
150.	**Author** Leopold P.L. O'Mahony M.J. Julie Lian X. Tilley A.E. Harvey B.G. Crystal R.G. **Title** Smoking is associated with shortened airway Cilia. **Source** PLoS ONE. 4 (12) , 2009. Article Number: e8157. Date of Publication: 2009.	
151.	**Author** Berntsen R. Nielsen E.W. **Title** Bronchoscopy in rural areas?. **Source** Pulmonary Medicine. , 2012. Article Number: 872327. Date of Publication: 2012.	
152.	**Author** McIntire, Maria [Author]; Shah, Neha D. [Author]; Kim, Anthony W. [Author]; Gattuso, Paolo [Author, Reprint Author; E-mail: paolo_gattuso@rush.edu]; Liptay, Michael J. [Author]. **Title** Cytologic Imprints of Giant Atypical Bronchopulmonary Carcinoid Tumor of the Lung With Extensive Oncocytic Component **Source** Diagnostic Cytopathology. 36(12). DEC 2008. 887-890.	
153.	**Author** Roth K. Hardie J.A. Andreassen A.H. Leh F. Eagan T.M.L. **Title** Predictors of diagnostic yield in bronchoscopy: A retrospective cohort study comparing different combinations of sampling techniques. **Source** BMC Pulmonary Medicine. 8 , 2008. Article Number: 2. Date of Publication: 26 Jan 2008.	
154.	**Author** Schramm M. Wrobel C. Born I. Kazimirek M. Pomjanski N. William M. Kappes R. Gerharz C.D. Biesterfeld S. Bocking A. **Title** Equivocal cytology in lung cancer diagnosis. **Source** Cancer Cytopathology. 119 (3) (pp 177-192), 2011. Date of Publication: 25 Jun 2011.	

155.	**Author** Schramm, Martin [Author]; Wrobel, Christian [Author]; Born, Ingmar [Author]; Kazimirek, Marietta [Author]; Pomjanski, Natalia [Author]; William, Marina [Author]; Kappes, Rainer [Author]; Gerharz, Claus Dieter [Author]; Biesterfeld, Stefan [Author, Reprint Author; E-mail: Stefan.Biesterfeld@med.uni-duesseldorf.de]; Boecking, Alfred [Author]. **Title** Equivocal Cytology in Lung Cancer Diagnosis Improvement of Diagnostic Accuracy Using Adjuvant Multicolor FISH, DNA-image cytometry, and Quantitative Promoter Hypermethylation Analysis **Source** Cancer. 119(3). JUN 25 2011. 177-192.	
156.	**Author** Lommatzsch, Steven E.; Martin, Richard J.; Good, James T. Jr **Title** Importance of fiberoptic bronchoscopy in identifying asthma phenotypes to direct personalized therapy.[Review] **Source** Current Opinion in Pulmonary Medicine.	
157.	**Author** Lommatzsch, Steven E.; Martin, Richard J.; Good, James T. Jr **Title** Importance of fiberoptic bronchoscopy in identifying asthma phenotypes to direct personalized therapy.[Review] **Source** Current Opinion in Pulmonary Medicine.	
158.	**Author** Chambers, Daniel C. [Author, Reprint Author; E-mail: daniel_chambers@health.qld.gov.au]; Hodge, Sandra [Author]; Hodge, Greg [Author]; Yerkovich, Stephanie T. [Author]; Kermeen, Fiona D. [Author]; Reynolds, Paul [Author]; Holmes, Mark [Author]; Hopkins, Peter M. A. [Author]. **Title** A novel approach to the assessment of lymphocytic bronchiolitis after Lung transplantation-transbronchial brush **Source** Journal of Heart & Lung Transplantation. 30(5). MAY 2011. 544-551.	
159.	**Author** Moreira, Andre L. 1; Thornton, Raymond H. 2 **Title** Personalized Medicine for Non-Small-Cell Lung Cancer: Implications of Recent Advances in Tissue Acquisition for Molecular and Histologic Testing.[Review] **Source** Clinical Lung Cancer. 13(5):334-339, September 2012.	Reviews (n=3)
160.	**Author** Dionisio J. **Title** Diagnostic flexible bronchoscopy and accessory techniques. **Source** Revista Portuguesa de Pneumologia. 18 (2) (pp 99-106), 2012. Date of Publication: April 2012.	
161.	**Author** El-Bayoumi, Ezzat M.D. 1; Silvestri, Gerard A. M.D., M.S., F.C.C.P. 1 **Title** Bronchoscopy for the Diagnosis and Staging of Lung Cancer.[Article] **Source** Seminars in Respiratory & Critical Care Medicine. Lung Cancer: Evolving Concepts. 29(3):261-270, June 2008.	

APPENDIX D: Literature Search History

The following search was performed on 2/1/2013 to encompass clinical reports on the use of cytology brushes in lung biopsy.

Ovid Search Results

Database(s): **Journals@Ovid Full Text** January 31, 2013**, Your Journals@Ovid, EBM Reviews - Cochrane Database of Systematic Reviews** 2005 to December 2012**, EBM Reviews - ACP Journal Club** 1991 to December 2012**, EBM Reviews - Database of Abstracts of Reviews of Effects** 4th Quarter 2012**, EBM Reviews - Cochrane Central Register of Controlled Trials** December 2012**, EBM Reviews - Cochrane Methodology Register** 3rd Quarter 2012**, EBM Reviews - Health Technology Assessment** 1st Quarter 2013**, EBM Reviews - NHS Economic Evaluation Database** 1st Quarter 2013**, BIOSIS Previews** 1993 to 2013 Week 09**, Embase** 1988 to 2013 Week 04**, Inspec** 1969 to 2013 Week 03**, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R)** 1946 to Present

Search Strategy:

#	Searches	Results
1	((Cytolog* or Cyto log* or airway* or air way* or biops* or bronch* or diaphragm* or laryn* or lung* or mediastin* or media stin* or pleur* or pneumo* or thorac* or thorax* or trache* or transbronch* or transdiaphragm* or translaryn* or transmediastin* or transmedia stin* or transpleur* or transpneumo* or transtrache* or windpipe* or wind pipe*) adj4 (Brush* or Microbrush*)).ab,kw,ac,ao,ap,bc,bt,ct,cb,cm,am,ci,cc,cw,dm,ec,xs,fs,tx,no,gc,ge,gn,gn,gw,go,gs,hy,ic,id,kf,hw,mc,sh,mq,mi,ms,nm,oi,or,oc,ot,oh,ps,pr,rn,rw,to,si,sq,st,sd,if,sn,ss,ts,tn,tw,ti,tr.	14874
2	(airway* or air way* or bilobectom* or (bleb* adj3 (emphyse* or emphysae*)) or bronch* or chest* or cordectom* or diaphragm* or epiglottidectom* or hemilaryn* or intercost* or inter cost* or laryn* or lobectom* or lung* or mediastin* or media stin* or (pect* adj3 deform*) or (phrenic* adj3 nerve*) or pleura* or ((pleuroperiton* or pleuro periton*) adj3 shunt*) or pneumo* or thorac* or thorax* or trache* or transbronch* or transdiaphragm* or translaryn* or transmediastin* or transmedia stin* or transpleura* or transpneumo* or transtrache* or windpipe* or wind pipe*).ti,ab.	3076141
3	biops*.ti,ab.	826395
4	(conference* or congress* or meeting* or poster* or symposia* or symposium* or (oral* and (abstract* or presentation* or session*)) or comment* or editorial* or letter* or note* or patent*).dt,lt,pt.	15525413
5	(1 and 2 and 3) not 4	1950
6	limit 5 to yr="2008 -Current" [Limit not valid in DARE; records were retained]	451
7	remove duplicates from 6	200
8	limit 7 to english language [Limit not valid in Journals@Ovid,Your Journals@Ovid,CDSR,ACP Journal Club,DARE,CCTR,CLCMR; records were retained]	176

Results (Kept 176 of 176)

APPENDIX E: Clinical Experience Data

(b) (4)

The following data set contains all Injuries and Deaths reported in MAUDE between January 1, 2008 and December 31, 2012 (See Table 7 for MAUDE search criteria).

MAUDE Data.xlsx

APPENDIX F

Post Market Clinical Follow-Up (PMCF) Evaluation Checklist

Risk Evaluation: superDimension Triple Needle Cytology Brush

(When answering the following questions, new is defined as the product having a new indication for use which is not cleared/approved for any other device in the market.)

Risk Criteria	Yes / No / NA
Innovation: Is the design of the device, the material, the principles of operation, the technology, or the medical indication/intended use new?	No
Does the severity of disease or application of the product have an impact on the performance of the product in a way that it may present additional harm to the patient?	No
Will this product be used on a sensitive target population or a new target population not previously considered?	No
Will this product be used on a risky anatomical location or a new anatomical location not previously considered?	No
Has there been a well known risk or a new risk identified from the literature?	No
Has there been a well known risk or a new risk identified of similar marketed devices?	No
Has there been any identification of an acceptable risk during pre-CE clinical trial, which should be monitored in a longer term and/or through a larger population?	No
Have any obvious discrepancies between the premarket follow-up timescales and the expected life of the product been identified?	No

If any of the above answers are yes, please document the PMCF activity to be conducted based off of a cross-function discussion.

"If all of the above the above questions result in a NO response, then it is determined that the long-term clinical data demonstrates safety and performance for its intended use. PMCF is not necessary because the purpose of PMCF has already been met."

If any of the above questions result in a YES response, please justify the reasoning for not conducting a PMCF. Consider referencing the appropriate Risk Management Report, risks considered acceptable in RMR may provide justification that no PMCF is needed.

Based on the assessment above, it has been decided that PMCF is needed. Yes (No)

If YES, then a cross-function team will meet to discuss what activity will be conducted in accordance with this procedure."

Clinical Affairs / Date

Quality / Date

Regulatory Affairs / Date

Clinician / Date

ATTACHMENT 4

Draft IFU and Packaging Labels and Modified 510(k) Summary Statement

- Triple Needle Brush IFU
- Draft SDTNB1000 Pouch Label
- Draft SDTNB1000 Box Label
- Draft SDTNB1500 Pouch Label
- Draft SDTNB1500 Box Label
- Modified 510(k) Summary Statement

superDimension™

Triple Needle Cytology Brush

Instructions For Use

REF SDTNB1000
REF SDTNB1500

Triple Needle Cytology Brush

READ CAREFULLY BEFORE USING

Symbols

Symbols are used to highlight safety points and other important information. The symbols may be found on packaging, labeling, or the instrument. The following symbols are used:


Consult instructions for use


WARNING: Indicates a potentially hazardous situation that – if not avoided – could result in death or serious injury


CAUTION: Indicates a potentially hazardous situation that could result in injury or damage to the device or equipment

Sterile using ethylene oxide


Single use


Do not use if package is opened or damaged


Use by

Batch code

Catalogue number

CAUTION: Federal law (USA) restricts this device to sale by or on the order of a physician

Device Description

The triple needle cytology brush is designed to provide the ideal combination of high specimen yield and ease of use. This device features Ethylene Tetrafluoroethylene (ETFE) sheathing and sharpened tips that can be used to penetrate tissue to obtain tissue or cell samples.

Safety

Indications for Use

For use through a flexible endoscope, or with the superDimension system, by physicians who are trained in endoscopic techniques for retrieving specimens from patients with endobronchial lesions, peripheral lung nodules, or lung masses.

Contraindications

None known.

Precautions

CAUTION: Excess pressure or force applied may cause damage to either the device or the biopsy channel.

CAUTION: Use of this device is restricted to devices or equipment with a biopsy channel minimum inside diameter of 2.08 mm (0.082 inch).

Instructions for Use

1. Open the pouch and remove the small tip protector from the cannula's distal end. **Save the product batch code (lot number) for future reference.**
2. Inspect for any functional abnormality. If any irregularities are noted, call Covidien for a return authorization number.
3. Gently slide the proximal end to ensure the device extends and retracts smoothly.

   NOTE: *Twisting or turning the thumb ring handle is not necessary for this device.*
4. Observe and note the position stops for the extended and retracted positions.
5. If aspiration is desired, securely attach a luer-lock syringe to the luer-lock fitting on the proximal end. To aspirate:

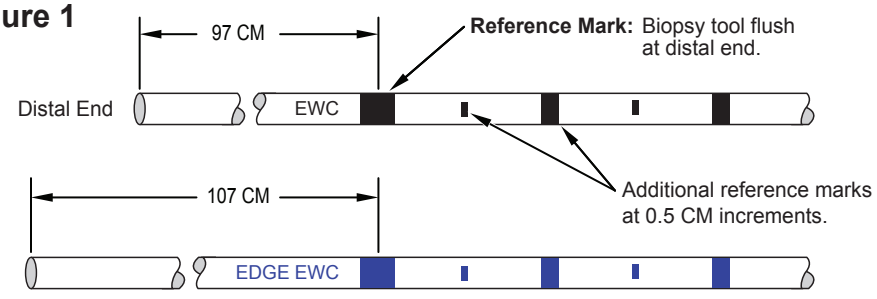
   5 (a). Insert the device's distal tip, in the retracted position, into the extended working channel (EWC) or other biopsy channel.

   5 (b). Use short, 2 cm strokes to advance the device until reaching the appropriate reference mark on the catheter body.

   NOTE: *Refer to Figure 1 for examples of the superDimension EWC black reference marks or Edge™ catheter blue reference marks.*
6. To obtain a specimen, use the thumb ring to extend the device. There is a 2 cm range of motion while moving the handle.
7. When the specimen is obtained, retract the device into the cannula. Remove the device from the biopsy channel keeping the device in the retracted position.
8. Hold the device's distal tip over prepared slides before retrieving the specimen.
9. Follow your health care facility sharps protocol and discard the contaminated device.

CAUTION: Covidien's single-use devices are designed and warranted for one-time use. To avoid potential infection or cross-contamination, do not reuse this device. Any device reuse is the end user's responsibility.

Figure 1



United States Office
superDimension, Inc
161 Cheshire Lane, Suite 100
Plymouth, MN 55441-5433, U.S.A.
Telephone: 1-800-387-9016
www.superdimension.com
Made in USA

EU Authorized Representative
Quality First International Limited
Suites 317/318, Burford Business Centre
11 Burford Road, Stratford
London, United Kingdom. E15 2ST
Telephone: +44-(0)208-221-2361
Fax: +44-(0)208-221-1912
www.qualityfirst.com

DLB00533-01 / PLB00431-01
2013-06

superDimension™

CONTENTS: 1

TRIPLE NEEDLE CYTOLOGY BRUSH

STERILE EO

Single use

Do not use if package is opened or damaged

Rx ONLY

Caution: Federal law (USA) restricts this device to sale by or on the order of a physician

Consult instructions for use

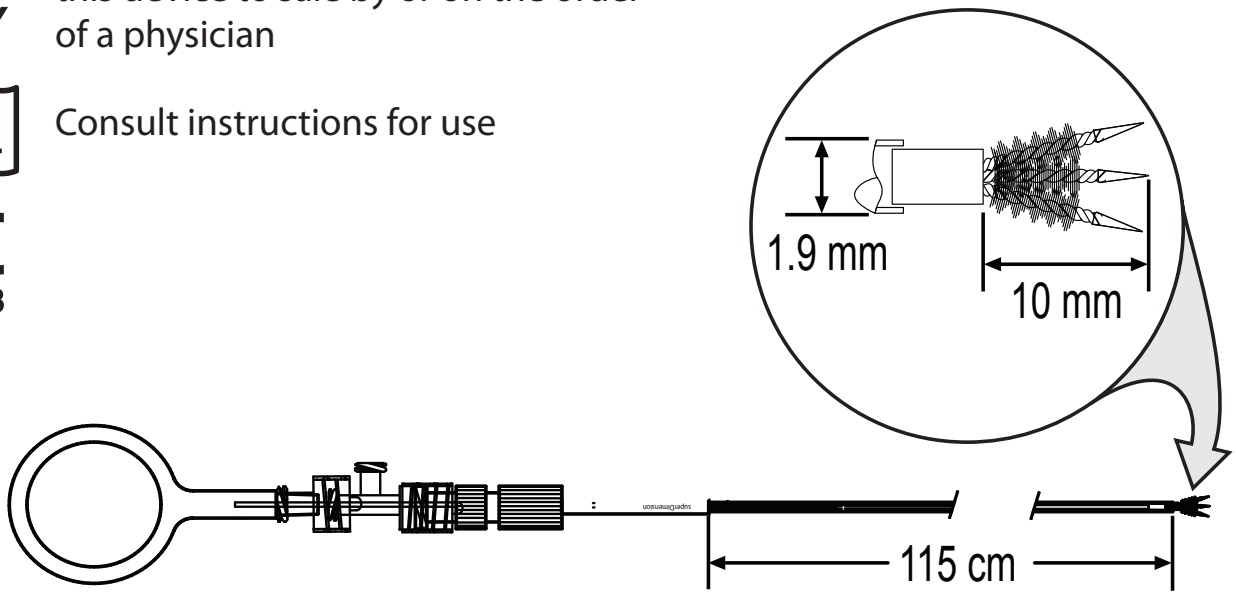
CE 0473

REF SDTNB1000

LOT XX##-##-###

YYYY-MM

Use by



DLB00530-01 PLB00428-01 2013-06

Manufactured for
superDimension, Inc.
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+1 888-586-4767 Made in USA

EC REP Quality First
International Limited
Suites 317/318, Burford Business Centre
17 Burford Road, Stratford London
E15 2ST United Kingdom
+44 - (0)208 - 2212361

superDimension™ TRIPLE NEEDLE CYTOLOGY BRUSH

Manufactured for
superDimension, Inc.
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Plymouth, MN 55441-5433 USA
+1 888-586-4767 Made in USA

EC REP Quality First International Limited
Suites 317/318, Burford Business Centre
11 Burford Road, Stratford London
E15 2ST United Kingdom
+44 - (0)208 - 2212361

REF SDTNB1000

LOT XX##-##-###

YYYY-MM
Use by

STERILE EO

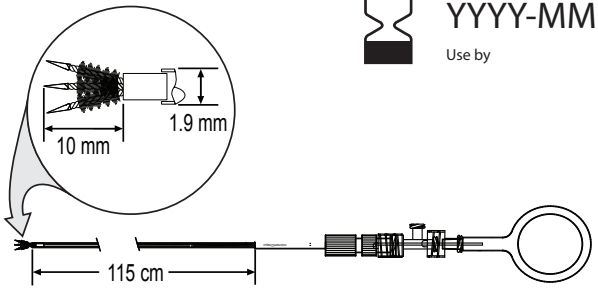
Single use

Do not use if package is opened or damaged

Rx ONLY Caution: Federal law (USA) restricts this device to sale by or on the order of a physician

Consult instructions for use

CE 0473



superDimension™ TRIPLE NEEDLE CYTOLOGY BRUSH CONTENTS: 10

Questions Contact FDA/CDRH/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

REF SDTNB1000

DLB00529-01 PLB00427-01 2013-06

superDimension™

CONTENTS: 1

TRIPLE NEEDLE CYTOLOGY BRUSH

STERILE EO

Single use

Do not use if package is opened or damaged

Rx ONLY

Caution: Federal law (USA) restricts this device to sale by or on the order of a physician

Consult instructions for use

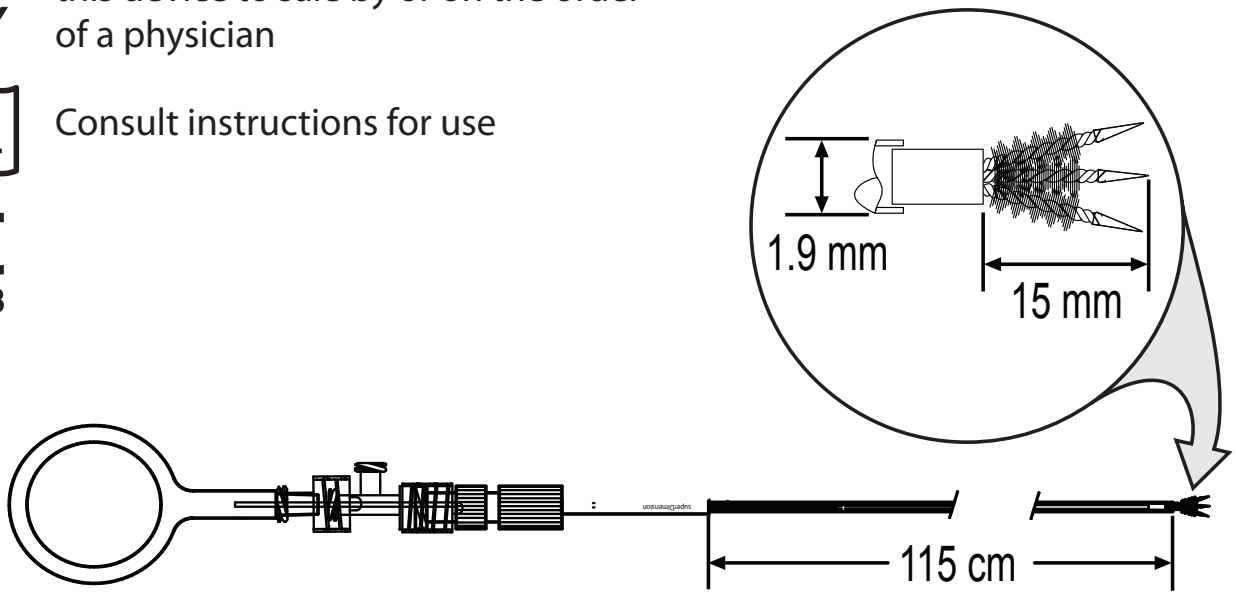
CE 0473

REF SDTNB1500

LOT XX##-##-###

YYYY-MM

Use by



DLB00532-01 PLB00430-01 2013-06

Manufactured for
superDimension, Inc.
161 Cheshire Lane, Suite 100
Plymouth, MN 55441-5433 USA
+1 888-586-4767 Made in USA

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International Limited
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+44 - (0)208 - 2212361

superDimension™ TRIPLE NEEDLE CYTOLOGY BRUSH

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EC REP Quality First International Limited
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11 Burford Road, Stratford London
E15 2ST United Kingdom
+44 - (0)208 - 2212361

REF SDTNB1500

LOT XX##-##-###

YYYY-MM
Use by

STERILE EO

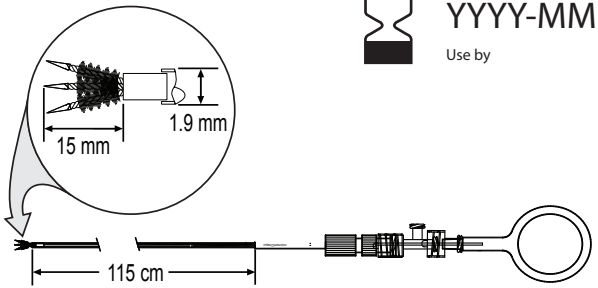
Single use

Do not use if package is opened or damaged

Rx ONLY Caution: Federal law (USA) restricts this device to sale by or on the order of a physician

Consult instructions for use

CE 0473



superDimension™ TRIPLE NEEDLE CYTOLOGY BRUSH CONTENTS: 10

Questions Contact FDA/CDRH/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

REF SDTNB1500

510(k) Summary
Covidien llc, dba superDimension Inc.
Traditional 510(k)
SuperDimension® Triple Needle Cytology Brush

Date Prepared:

9/27/2013

510(k) Applicant:

Deborah Fleetham
Manager Regulatory Affairs
Covidien llc, formerly registered as superDimension Inc.
161 Cheshire Lane Suite 100
Plymouth, MN 55441 U.S.A.
Ph: 763-210-4091
Fax: 763-210-4098
Email : deborah.fleetham@covidien.com

Name of Device :

Trade Name :	SuperDimension® Triple Needle Cytology Brush
Common Name:	Bronchial Biopsy Brush
Classification Name:	Brush, Biopsy, Bronchoscope (non-rigid) 21 CFR Part 874.4680
Product code:	BTG

Equivalent Legally-Marketed Device:

K834402 Gastrointestinal Sheath Brush (KOG) by Hobbs Medical, Inc.

K944650 Wang Bronchial Needle Brush (EOQ) by ConMed

Description:

The SuperDimension® Triple Needle Cytology Brush is designed for use with standard bronchoscopes or with the superDimension system. The SuperDimension® Triple Needle Cytology Brush is designed to provide high specimen yield and ease of use. This device features Ethylene Tetrafluoroethylene (ETFE) sheathing and sharpened tips that can be used to rough up tissue to obtain a sample of tissue/cells. The SuperDimension® Triple Needle Cytology Brush is similar to currently marketed cytology brushes except that it has three smaller brushes in place of one larger brush.

Intended Use:
To be utilized through a flexible endoscope or the superDimension system by physicians who are trained in endoscopic techniques for retrieving specimens from patients with endobronchial lesions, peripheral lung nodules, or lung masses.

Summary of Characteristics Compared to Predicate Device:
The use of the SuperDimension® Triple Needle Cytology Brush is equivalent to the predicate devices in that these devices are all advanced into the body either individually or through a separate catheter channel. Once they reach the target biopsy site, a sample is taken from the desired site. While the predicate devices each contain one larger brush, the SuperDimension® Triple Needle Cytology Brush contains three smaller brushes. Once the sample is obtained, the brushes are retracted back into the sheath and the entire tool is withdrawn from the body.

The SuperDimension® Triple Needle Cytology Brush and the predicate devices are all single use, sterile devices. The shaft length, materials, and function are substantially similar with the same technological function.

Performance Data:
In-vitro testing has been performed and all components, subassemblies, and /or full devices met the required specifications for the completed tests.

Clinical Data:
Clinical tests were not required to validate the design of the SuperDimension® Triple Needle Cytology Brush due to the extensive history of similar devices.

Conclusion:
Covidien llc has demonstrated that the proposed SuperDimension® Triple Needle Cytology Brush is substantially equivalent to Gastrointestinal Sheath Brush (KOG) by Hobbs Medical, Inc. K834402, and the Wang Bronchial Needle Brush (EOQ) by ConMed K944650.

ATTACHMENT 5
AAMI TIR 28:2009 Adoption Questionnaire

(b) (4)

(b) (4)

(b) (4)

(b) (4)

(b) (4)

(b) (4)

(b) (4)

(b) (4)

Document No.:	[redacted]	Revision (b) (4)
Document Title:	Triple Needle Brush Retraction of Damaged Brushes Evaluation Report	Effective [redacted]
Owner:	Research & Development	Page 1 of 14
Author:	(b) (4), (b) (6) [redacted]	

Triple Needle Brush Retraction of Damaged Brushes Evaluation Report

Table of Contents

1.0 PURPOSE

In order to ensure that, if damaged, cytology brushes can still be safely withdrawn from the lung, these tests evaluated the force needed to retract twisted, malformed, or bent brushes into the outer sheath of both lengths of the Covidien triple needle tip brushes, the Hobbs Biopsy Brush, and the ConMed needle tip brush.

This report will detail the results of the evaluation of the following parts:

(b) (4)

2.0 DEFINITIONS / ACRONYMS / ABBREVIATIONS

TNB – Triple needle brush
HMI – Hobbs Medical Inc.
EWC – Extended working channel
N – Newton
SD - superDimension

3.0 REFERENCES

(b) (4)

4.0 SUMMARY OF TESTING ACTIVITIES

(b) (4)

5.0 TEST ENVIRONMENT

(b) (4)

6.0 TEST EQUIPMENT / MATERIALS / TOOLS

(b) (4)

7.0 TEST ARTICLES

(b) (4)

(b) (4) Testing, (b) (4) Materials

(b) (4) Testing, (b) (4) Materials

(b) (4) Testing, (b) (4) Materials

(b) (4) Testing, (b) (4) Materials

(b) (4) Testing, (b) (4) Materials

(b) (4) Testing, (b) (4) Materials

(b) (4) Testing, (b) (4) Materials

(b) (4) Testing, (b) (4) Materials

(b) (4) Testing, (b) (4) Materials

(b) (4) Testing, (b) (4) Materials

(b) (4) Testing, (b) (4) Materials

ATTACHMENT 7

- (b) (4) User Validation Test Protocol for the Triple Needle Tipped Cytology Brush
- User Validation Test Report for the Triple Needle Tipped Cytology Brush

User Validation Test Protocol for the Triple Needle Tipped Cytology Brush

Contents

		Revision (b) (4)
Document Title:	User Validation Test Protocol for the Triple Needle Tipped Cytology Brush	Effective
Owner:		
Author:	(b) (4), (b) (6)	

1.0 Purpose

This document is the user validation test protocol for the triple needle tipped cytology brush. The document describes the test environment, test equipment, and actual test protocol that will be used to perform the user validation. The validation will also serve to validate the proposed instructions for use.

The scope of this validation is the 10 mm and 15 mm triple needle cytology brushes manufactured by Hobbs Medical for Covidien llc.

2.0 Definitions / Acronyms / Abbreviations

EWC	Extended Working Channel
sD	superDimension
N/A	Not Applicable
TNB	Triple Needle Brush
ILM	Inflatable Lung Model
tbbx	Transbronchial biopsy

3.0 References

(b) (4)

4.0 Summary of Testing Activities

(b) (4)

(b) (4) Testing, (b) (4) Materials

(b) (4) Testing, (b) (4) Materials

(b) (4) Testing, (b) (4) Materials

(b) (4) Testing, (b) (4) Materials

(b) (4) Testing, (b) (4) Materials

Appendix C
Physician Survey

Circle Navigation #: 1 2 3 4 5 6 7 8 9

1	Rate the ability of the device to reach the target location.	☐ Unacceptable ☐ Acceptable ☐ Very well
2	How well does the device demonstrate sampling within and adjacent to airway tree?	☐ Unacceptable ☐ Acceptable ☐ Very well
3	Qualitatively, did the test device collect less, the same, or more tissue as compared to the ConMed device?	☐ Less ☐ Same ☐ More
4	Did the device retract into its sheath and into the EWC?	☐ Yes ☐ No ☐ N/A
5	If the device failed to retract into its sheath, do you have other acceptable options to safely remove the device without damaging healthy tissue?	☐ Yes ☐ No ☐ N/A
6	Is it possible to safely gauge the position of the needle tips relative to the pleural boundary?	☐ Yes ☐ No ☐ N/A

Comments:

Physician Name: _____

Physician Signature: _____

Date: _____

Appendix D
Physician Summary Questions

1	Is the Triple Needle Cytology Brush generally safe to use relative to the benefits of this type of procedure?	☐ Yes	☐ No	☐ N/A
2	Is the safety of the triple needle tipped cytology brush generally equivalent to the ConMed needle brush?	☐ Yes	☐ No	☐ N/A
3	Was the pig lung an adequate model for assessing the safety of the device?	☐ Yes	☐ No	☐ N/A
4	Is there adequate visibility of all brush locations using fluoroscopy?	☐ Yes	☐ No	☐ N/A
5	Were the test devices compatible with both the conventional and Edge technology platforms?	☐ Yes	☐ No	☐ N/A

Comments:

Physician Name: _____

Physician Signature: _____

Date: _____

(b) (4)

		Revision	(b) (4)
Document Title:	User Validation Test Report for the the Triple Needle Tipped Cytology Brush	Effective	
Owner:			
Author	(b) (4), (b) (6)		

Table of Contents

	[redacted]	Revisio
Document Title:	User Validation Test Report for the the Triple Needle Tipped Cytology Brush	Effectiv
Owner:		
Author	(b) (4), (b) (6)	

1.0 PURPOSE

This document is the user validation report for the Triple Needle Tipped Cytology Brush. The document describes the results of the user validation testing.

The user validation purpose was to demonstrate that the Triple Needle Tipped Cytology Brush conforms to user needs and intended uses. This testing focused on the 10 mm and 15 mm Triple Needle Tipped Cytology Brushes.

The testing activity was performed under user simulated conditions as defined in the test protocol, at the Covidien llc facility in Plymouth, MN. The Triple Needle Tipped Cytology Brush devices were manufactured using final design specifications. Testing activity included target location planning followed by Electromagnetic Navigation Bronchoscopy and biopsy sampling. (b) (4)

(b) (4)

(b) (4)

(b) (4) Testing, (b) (4) Materials

(b) (4) Testing, (b) (4) Materials

(b) (4) Testing, (b) (4) Materials

(b) (4) Testing, (b) (4) Materials

(b) (4) Testing, (b) (4) Materials

(b) (4) Testing, (b) (4) Materials

(b) (4) Testing, (b) (4) Materials

6.0 CONCLUSION

This design validation was performed under defined operating conditions that simulate the Bronchoscopy Suite. The test devices represented the final design specifications.

The physician successfully completed the requirements of the design validation. There were no anomalies that prevented the study from being completed efficiently and successfully. In conclusion, the design validation study ensured that the devices and proposed labeling conform to defined user needs and intended uses. The physician was able to use the 10 mm and 15 mm Triple Needle Cytology Brushes and successfully biopsy all target locations.

The post procedural photographs (see appendix) of each tool demonstrate that the brush tips are not damaged by aggressive sampling or worst case torque conditions. In all cases, the cytology brushes were able to be safely retracted after excessive torqueing and sampling. All brushes were able to be adequately visualized in this model. No additional potential hazards were identified.

The protocol discrepancies did not negatively impact the conclusion of the study.

Table 3 below demonstrates the fulfillment of the protocol specified customer requirements. The applicable requirements were taken from the customer requirements documents.

(b) (4) Design Validation Reports [redacted]

(b) (4) Design Validation Reports

(b) (4) Design Validation Reports

(b) (4) Design Validation Reports

(b) (4) Design Validation Reports

(b) (4) Design Validation Reports

(b) (4) Design Validation Reports

(b) (4) Design Validation Reports

(b) (4) Design Validation Reports

ATTACHMENT 8

(b) (4) Design Verification Test Report for Supplemental Testing on Needle Brush (Bristle Condition and Aspiration Port)

Document No.:		Revisio (b) (4)
Document Title:	Design Verification Test Report for Supplemental Testing on Needle Brush (Bristle Condition and Aspiration Port)	Effecti
Owner:	Research and Development	Page 1 of 4
Author:	(b) (4), (b) (6)	

Design Verification Test Report for Supplemental Testing on Needle Brush (Bristle Condition and Aspiration Port)

Table of Contents

1.0 PURPOSE

The purpose of this report is to report the results of the supplemental testing and to demonstrate that the Triple Needle Brush meets the following three specifications per specification requirements documents.

(b) (4)

2.0 REFERENCES

(b) (4)

3.0 TEST DATA

(b) (4)

4.0 ANALYSIS OF RESULTS

(b) (4)

(b) (4)

5.0 PROTOCOL DISCREPANCIES

There were no protocol discrepancies.

6.0 CONCLUSION

(b) (4)

(b) (4)

With an 80% confidence and 85% reliability level, acceptance was demonstrated with 20 parts and 1failure.

(b) (4)

All device subassemblies tested met acceptance criteria defined in test protocol. Either direction of the tip grind at Hobbs medical would be acceptable for manufacturing.

Summary

With an 80% confidence and 85% reliability level, acceptance was demonstrated for the following design specificatio (b) (4)

(b) (4)

ATTACHMENT 9

(b) (4) Design Validation Test Protocol for Triple Needle Tipped Cytology Brush
Design Validation Test Report for Triple Needle Tip Cytology Brush, Tissue Collection

Design Validation Test Protocol for Triple Needle Tipped Cytology Brush

Table of Contents

Document No.:	[redacted]	Revision:	(b) (4)
Document Title:	Design Validation Test Protocol for Triple Needle Tipped Cytology Brush	Effective:	[redacted]
Owner:			
Author:	(b) (4)		

1.0 PURPOSE

This document is an additional design validation test for the triple needle tipped cytology brush. The document describes the test environment, test equipment, and users to perform the design validation for the triple needle tipped cytology brush.

2.0 DEFINITIONS / ACRONYMS / ABBREVIATIONS

EWC	Extended Working Channel
sD	superDimension
N/A	Not Applicable
TNB	Triple Needle Brush
SLM	Simplified Lung Model

3.0 REFERENCES

(b) (4) [redacted]

4.0 SUMMARY OF TESTING ACTIVITIES

(b) (4) [redacted]

5.0 TEST ENVIRONMENT

The test is performed within Covidien premises. This test environment will simulate a standard operating, endoscopy, and bronchoscopy room.

Document No.:	[redacted]	Revision	(b) (4) [redacted]
Document Title:	Design Validation Test Protocol for Triple Needle Tipped Cytology Brush	Effective	
Owner:			
Author:	(b) (4) [redacted]		

6.0 TEST EQUIPMENT / MATERIALS / TOOLS

Table 1: Test Equipment

(b) (4) [redacted]

The test articles and test equipment are detailed above (See section 6.0 above).

8.0 SAMPLE SIZE DETERMINATION

(b) (4) [redacted]

(b) (4) Testing, (b) (4) Materials

(b) (4) Testing, (b) (4) Materials

(b) (4) Testing, (b) (4) Materials

12.0 TEST FORMS

SDTNB1000				
1	Rate the ability of the Triple Needle Cytology Brush to collect tissue.	☐ Unacceptable	☐ Acceptable	☐ Very well
2	Qualitatively, did the Triple Needle Cytology Brush collect less, the same, or more tissue as compared to the predicate device?	☐ Less	☐ Same	☐ More
3	Did the device retract into its sheath and into the EWC?	☐ Yes	☐ No	☐ N/A

Number of times SDTNB1000 pushed into the simulated lesion: _____

SDTNB1500				
1	Rate the ability of the Triple Needle Cytology Brush to collect tissue.	☐ Unacceptable	☐ Acceptable	☐ Very well
2	Qualitatively, did the Triple Needle Cytology Brush collect less, the same, or more tissue as compared to the predicate device?	☐ Less	☐ Same	☐ More
3	Did the device retract into its sheath and into the EWC?	☐ Yes	☐ No	☐ N/A

Number of times SDTNB1500 pushed into the simulated lesion: _____

ConMed NB-120				
1	Rate the ability of the ConMed Brush to collect tissue.	☐ Unacceptable	☐ Acceptable	☐ Very well
2	Qualitatively, did the ConMed brush collect less, the same, or more tissue as compared to the test device?	☐ Less	☐ Same	☐ More
3	Did the device retract into its sheath and into the EWC?	☐ Yes	☐ No	☐ N/A

Number of times the ConMed brush was pushed into the simulated lesion: _____

Comments:

Printed Name: _____

Signature: _____

Date Completed: _____

12.1 TEST ARTICLE/EQUIPMENT FORM

(b) (4) Testing, (b) (4) Materials

Initials /Date _____

	[redacted]	Revision (b) (4)
Document Title:	Design Validation Test Report for Triple Needle Tip Cytology Brush, Tissue Collection	Effectiv [redacted]
Owner:	Research and Development	Page 1 of 9
Author:	(b) (4), (b) (6) [redacted]	

Design Validation Test Report for Triple Needle Tip Cytology Brush Tissue Collection

Table of Contents

(b) (4) Design, (b) (4) Testing

1.0 PURPOSE

The purpose of this report is to present test results against the referenced protocol, when using the Triple Needle Brush products compared to the ConMed Needle brush.

2.0 REFERENCES

(b) (4) [redacted] Design Validation Test Protocol for Triple Needle Tip Cytology Brush Tissue Collection

(b) (4) [redacted]

(b) (4) Testing, (b) (4) Design

(b) (4) Testing, (b) (4) Design

		Revision	(b) (4)
Document Title:	Design Validation Test Report for Triple Needle Tip Cytology Brush, Tissue Collection	Effective	
Owner:			
Author:	(b) (4), (b) (6)		

4.0 ANALYSIS OF RESULTS

The acceptance criteria for the Triple Needle Brush were defined in the protocol as:

- The test articles successfully pass through the channel (Edge EWC) into the simulated lung tissue
- The test articles contain visible evidenc (b) (4) the cytology brushes upon withdrawal.

(b) (4)

The test articles were the two sizes of the triple needle brush models. There were no criteria for the competitive, predicate devices which were included for comparative purposes only. All acceptance criteria specified in the protocol have been met.

(b) (4)

(b) (4) ll brushes retracted back into their sheaths and were removed, causing no difficulties when subjected to normal use.

5.0 PROTOCOL DISCREPANCIES

N/A

6.0 CONCLUSION

The Triple Needle Brush product collected tissue from the simulated lung material while being used through the Edge catheter when tested per the protocol. There was no attempt to quantify the amount of tissue due to the complexity of these techniques. The predicate devices tested as part of the above protocol were for comparative purposes and did not have any formal acceptance criteria.

The table below shows how the customer requirements were fulfilled by this testing.

(b) (4)

	[redacted]	Revisio[redacted] (b) (4)
Document Title:	Design Validation Test Report for Triple Needle Tip Cytology Brush, Tissue Collection	Effecti[redacted]
Owner:		
Author:	(b) (4), (b) (6) [redacted]	

7.0 APPENDIX A

(b) (4)
[redacted]

(b) (4) Testing, (b) (4) Design

(b) (4) Testing, (b) (4) Design

ATTACHMENT 10

- Needle Tipped Cytology Brush: Characterization of Deployed Brush "Spread

	[redacted]	Revisio
Document Title:	Needle Tipped Cytology Brush: Characterization of Deployed Brush "Spread"	Effectiv
Owner:	R&D	Page 1 of 9
Author:	(b) (4), (b) (6)	

(b) (4)

1.0 PURPOSE

The purpose of this document is to characterize the "spread" of the tips of the needle tipped cytology brushes when deployed in air.

2.0 DEFINITIONS / ACRONYMS / ABBREVIATIONS

2.1 P/N: part number
2.2 TNB: Triple Needle – Tipped Cytology Brush P/N SDTNB1000 and SDTNB1500

3.0 REFERENCES

3.1 N/A

4.0 TEST ENVIRONMENT

(b) (4)

5.0 TEST EQUIPMENT / MATERIALS / TOOLS

(b) (4)

(b) (4) Testing Methods, Diagrams & Results

(b) (4) Testing Methods, Diagrams & Results

(b) (4) Testing Methods, Diagrams & Results

(b) (4) Testing Methods, Diagrams & Results

(b) (4) Testing Methods, Diagrams & Results

(b) (4) Testing Methods, Diagrams & Results

(b) (4) Testing Methods, Diagrams & Results

(b) (4) Testing Methods, Diagrams & Results