

**Research Article**

**Comparison of bronchial biopsy, broncho alveolar lavage (BAL), brush cytology and imprint cytology in suspected cases of lung cancer**

**Tarun P Kotadia**<sup>\*1</sup>, Jasmin H Jasani<sup>2</sup> and Parul N Vekaria<sup>3</sup>

<sup>1</sup>Assistant Professor, Department of Pathology, GMERS Medical College and Hospital, Dharpur, Patan.

<sup>2</sup>Associate Professor, Department of Pathology, S.B.K.S.M.I. & R.C., Piparia.

<sup>3</sup>Assistant Professor, Department of Pathology, Govt. Medical College Rajkot

**\*Correspondence Info:**

Dr. Tarun Kotadia

127/Shyam Satya Bunglows,

B/H Satyev hospital, Chandkheda, Ahmedabad-, PIN -382424

E mail : [kotadia\\_taru@yahoo.co.in](mailto:kotadia_taru@yahoo.co.in)

**Abstract**

**Background:** The use of cytological methods in the diagnosis of malignant lesions of the respiratory tract has been generally acclaimed as one of its most successful applications. Flexible fiberoptic bronchoscopy revolutionized respiratory cytology, as bronchial brushings, broncho-alveolar lavage and bronchial forceps biopsy became more easy, accessible and popular, shifting the emphasis from diagnosis of advanced malignancy in inoperable patients to the use of cytology as a first line diagnostic and management tool. Respiratory tract cytology is well established throughout the world as a diagnostic procedure in the evaluation of patient with suspected lung malignancy.

**Methodology:** The present study comprises of bronchoscopic cytology and histology of bronchial biopsy in 80 patients suspected of lung tumors. The study was carried out in the department of pathology M.P. shah medical college and the samples of the bronchoscopic material were received from tuberculosis and chest department of G.G hospital Jamnagar.

**Results:** Out of 80 patients 66 were found to be malignant. Some of the suspicious lesions turned out to be malignant in biopsy. In the carcinoma of lung squamous cell carcinoma was the most common carcinoma (39.39% ) followed by adenocarcinoma (21.21%) small cell carcinoma 13.63% and large cell carcinoma 7.57 %, majority of the cases 77.5 % were male predominant.

**Conclusion:** Pulmonary cytology is an important, basic diagnostic tool for the detection of lung cancer, that too in early diagnosis. Fibroptic bronchoscopy is an easy, OPD procedure which is minimally invasive and without any risk. It provides direct visualization of respiratory tract as well as lesion proper and variety of specimens can be collected.

**Keywords:** Bronchial biopsy, Broncho alveolar lavage (BAL), Brush cytology and Imprint cytology, Lung cancer

**1. Introduction**

Pulmonary cancers have taken place as most common malignant disease affecting larger population with continuous rising incidences and currently recognized as serious health problem because of its high morbidity and mortality and poor prognosis<sup>1</sup>.

The use of cytological method In the diagnosis of malignant lesions of respiratory track has been generally acclaimed as one of its most successful applications<sup>2</sup>.

Tumors of lung as noted by alder, were a rarity in the beginning of the twentieth century. There was no way for alder to foresee that in the coming years cancer of lung would show a astonishing 15 fold increase in males and 10 fold

increase in females. In females, cancer of lung is expected to surpass the deaths due to cancer of breast<sup>3</sup>.

The global incidence of lung cancer is increasing at the rate of 0.5 % per year and is the leading cause of death in most countries. Smoking is considered to be the cause of 85 % of deaths due to lung cancer death<sup>4,5</sup>.

The result of the American society's prevention study II indicates that the risk of lung cancer has doubled among men and more than quadrupled in females, in comparison with prior estimates. Rosenow stated that even if all the smokers stopped smoking immediately, no decline in lung cancer incidences for 5 – 15 years<sup>6</sup>.

The age and sex distribution for various histological subtypes of lung has been shifted during the past several decades<sup>7</sup>.

So, early detection is deadly needed in present scenario with clinical symptoms , x- ray chest , sputum cytology and tumor markers which can support the evidence of tumor by histological cell typing . therefore endoscopies and biopsies become inevitable since the advent of flexible fiberoptic bronchoscope by ikeda in the early 1970<sup>8</sup>.

Accuracy in the diagnosis of lung tumors has increased with the introduction of radiological guided per cutaneous transthoracic needle biopsy . Though the histological diagnosis of lung cancer from these specimens is considered definitive it is useful to have an earlier indication as o the presence of malignancy and the cytomorphological analysis of touch imprint smears made from core biopsies of the lesions might advance this<sup>9</sup>.

Thoractomy followed by removal of mass confirmed further for definitive diagnosis where thoracic surgeon and unit is available, raises the confidence level of the pathologist with compliance of the procedure.

## **2. Material and Method**

The present study compromises of bronchoscopic cytology and histology of bronchial biopsy in 80 patients suspected of lung tumors. The study was carried out in the department of pathology M.P. shah medical college and the samples of the bronchoscopic material were received from tuberculosis and chest department of G.G hospital Jamnagar

Total 80 patients clinically suspected of lung cancer were selected for cytological and histological study during the period of Nov 2004 to Nov 2006

The bronchoscopy was performed by flexible fibreoptic bronchoscope in tuberculosis and chest department in G.G hospital Jamnagar

## **3. Imprint Cytology**

### **3.1 Procedure**

The specimen of bronchial biopsy, before putting in a formalin bottle, was put on a clear glass slide, with the help of the other clear slide the imprint of biopsy was taken.

The side of the biopsy than changed and another imprint was taken on the same previous slide but on the other side.

The smears were fixed with 95% ethyl alcohol for 15 minutes. The well fixed slides were stained with haematoxylin and eosin.

The same biopsy bit was subjected for routine paraffin sections and stained by haematoxylin and eosin stain and histopathological correlation was done on subsequent days.

Fixed smears of TBNA and brush smears, collected by chest physician at T.B and chest department , were received and stained .

### **3.2 Staining**

Haematoxylin and eosin and papanicolaou stain have been used.

## **4. Observations and Result**

The present study comprises of 80 patients of suspected lung cancer during the period of Nov 2004 to Nov 2006. The patients included in this study had suspicious radiological as well as clinical findings of lung cancer with sputum

examination, suspicious for malignant cells. The study is of bronchoscopic specimens i.e is bronchial biopsy and its imprint cytology , bronchial brushing and TBNA.

#### 4.1 Diagnosis yeild for positivity of malignancy by various methods

In the present study, bronchoscopy was performed in 80 cases and bronchial biopsy specimens were studied in 80 cases. Touch preparation were examined in all the 80 cases. TBNA collection were received in 50 cases and brush smears were received in 42 cases. The cases where bronchial biopsy was not taken were excluded from the study

Material yield by various cytological technique obtained through bronchoscope and diagnostic positivity for malignancy observed as follows:

**Table : 01 Material yield and diagnostic positivity for malignancy by various bronchoscopic techniques :**

Techniques	No of specimens	Inadequate material no of cases	Material yield no of cases	Positive for malignancy no of cases
Brush	42	07	35 (83.3 % )	27
TBNA	50	13	37 (74.0%)	26
IMPRINT	80	04	76 (95%)	58
Biopsy	80	06	74 (92.5%)	66

Thus mentioned in the above table maximum material yield (95%) was in the imprint smear , followed by brush cytology (83.3 % ) . Biopsy material found to be inadequate as mentioned in the table (92.5 % ) this cases confirmed by other modalities, particularly imprint smears.

**Table 02 : Showing cytological findings by various techniques**

NO	CATEGORY	BRUSH n=42	TBNA n=50	IMPRINT n = 80	BIOPSY n=80
1	Definitive malignancy	27	26	58	66
2	Suspicious for malignancy	04	05	06	02
3	Dysplasia	02	02	04	02
4	Non malignant	02	04	08	04
5	Inadequate	07	13	04	06

Out of 80 patients 66 were found to be malignant. Some of the suspicious lesions turned out to be malignant in biopsy. Some of the smears which were found to be reactive due to irritation and chronic infection. All the lesions were classified accordingly to their cytomorphology and histology as mentioned in the table III.

**Table: 03 Incidence of various types of lung tumors**

No	Type of tumor	No of cases	Percentage %
1	squamous cell carcinoma	26	39.39
2	Adenocarcinoma	14	21.21
3	Small cell carcinoma	09	13.63
4	Large cell carcinoma	05	7.57
5	Bronchiole alveolar carcinoma	03	4.54
6	Adenosquamous carcinoma	02	3.03
7	Metastatic carcinoma	04	6.06
8	Undifferentiated carcinoma	03	4.54
	Total	66	100

From table No.3, it was observed that squamous cell carcinoma was the most common carcinoma (39.39% ) followed by adenocarcinoma (21.21%) small cell carcinoma 13.63% and large cell carcinoma 7.57 %

**Table :04 Age incidence in different carcinomas**

NO	LUNG CANCER	31-40	41-50	51-60	61-70
1	Squamous cell carcinoma	01	01	10	14
2	Small cell carcinoma	01	01	02	05
3	Adenocarcinoma	-	03	06	05
4	Bronchiolo alveolar carcinoma	-	-	03	-
5	Large cell carcinoma	01	-	01	03
6	Adenosquamous carcinoma	-	-	01	01
7	Metastatic carcinoma	-	-	04	-
8	Undifferentiated carcinoma	01	-	-	02
	Total	04	05	27	30

From table no 04, observed that , majority of the cases were in the 6<sup>th</sup> and 7<sup>th</sup> decade of life Malignancy was common in the 6<sup>th</sup> and 7<sup>th</sup> decade for primary lesion while metastatic lesion were common in 6<sup>th</sup> decade of life

**Table : 05 Overall gender incidence in 80 cases of study**

No	Sex of the Patients	No of Cases	Percentage
1	Male	62	77.5
2	Female	18	22.5
	Total	80	100%

From table no 05 , observed that , majority of the cases 77.5 % were male predominant.

**Table :06 Positive history of smoking (N= 80)**

No	History of smoking	No of cases	M	F	Percentage
1	Positive history of smoking	67	62	05	83.75
2	Negative history of smoking	13	05	08	16.25
	Total	80	13	100	

From Table no 06 Shows out of 80 patients studied, 67 had positive history of smoking. 62 were Male and 05 were female.

**Table :07 Positivity history of smoking in lung cancer patient (N =66)**

No	History of smoking	No of Patient	Percentage
1	Postive history of smoking	58 (55M +3F)	87.88
2	Negative history of smoking	08	12.12
	Total	66	100

From table no 07 shows out of 66 lung cancer patients, 58 (87.88%) patients had positive history of smoking. 3 of them were female.

**Table :08 Statistical analysis of various bronchoscopy techniques**

Technique	TP	FP	TN	FN	Sensitivity	Specificity	PVPR	PVNR	Accuracy Rate
BRUSH	23	03	06	03	88.46	66.67	88.46	66.67	82.85
TBNA	22	05	08	02	91.60	61.53	81.48	80.8	81.08
IMPRINT	62	02	15	01	98.41	88.23	96.87	93.75	92.50
BIOPSY	51	00	13	02	96.83	100	100	86.70	97.37

From table no 08 , it was observed that imprint cytology had highest sensitivity (98.41%) and highest PVNR (93.75%), while bronchial biopsy had 96.83 % sensitivity and 86.70 % PVNR.

**Table : 09 Statistical analysis of various bronchoscopy techniques**

Technique	TP	FP	TN	FN	Sensitivity	Specificity	PVPR	PVNR	Accuracy Rate
BRUSH	23	03	06	03	88.46	66.67	88.46	66.67	82.85
TBNA	22	05	08	02	91.60	61.53	81.48	80.8	81.08
IMPRINT	62	02	15	01	98.41	88.23	96.87	93.75	92.50
BIOPSY	51	00	13	02	96.83	100	100	86.70	97.37

TP : TRUE POSITIVE; TN : TRUE NEGATIVE; FP : FALSE POSITIVE; FN : FALSE NEGATIVE; PVPR: PREDICTIVE VALUES OF POSITIVE RESULTS; PVNR : PREDICTIVE VALUES OF NEGATIVE RESULT

## 5. Discussion

Because primary and secondary tumors of lung are such a frequent phenomenon, we must find reliable diagnostic methods with a high yield of positive results and accurate identification of the tumor type.

**Table :-10 Percentage incidence of various types of lung cancers**

Author	Squamous cell carcinoma	Adeno. carcinoma	Bronchiolo Alveolar carcinoma	Small cell carcinoma	Large cell carcinoma	Undiff. carcinoma	Others
Agarwal et al <sup>10</sup>	55	21.5	1.08	10.88	-	5.89	5.65
Rosell et al <sup>11</sup>	37.8	14.2	2.86	11.0	8.50	-	7.34
Popp et al <sup>12</sup>	31.57	8.23	3.53	8.05	-	3.20	-
Paulose et al <sup>13</sup>	40.0	15.8	3.94	15.54	5.7	-	8.20
Joos et al <sup>14</sup>	34.45	18.2	5.0	11.10	10.1	-	-
Adnan et al <sup>15</sup>	31.57	25.3	-	-	12.4	7.2	5.4
Present study	39.39	21.21	4.54	13.63	7.57	4.54	6.06

From the above table, it was observed that the squamous cell carcinoma was the most common type of lung cancer (39.39%) followed by Adenocarcinoma (21.21%) and Small cell carcinoma (13.63%) which is quite comparative with other studies.

**Table : 11 Showing statistical comparison of bronchial biopsy**

Author	Sensitivity	specificity	PPV	NPV	Accuracy rate
Matsuda et al <sup>16</sup>	-	98.0	-	-	95.0
Adnan et al <sup>15</sup>	90.5	-	-	84.0	-
Rosell et al <sup>11</sup>	-	95.0	-	-	-
Govert et al <sup>17</sup>	95.0	-	97	-	95.7
Paulose et al <sup>13</sup>	85.0	100	-	-	-
Present study	96.83	100	100	86.70	93.37

The above table shows that, the sensitivity, specificity and accuracy rate of bronchial biopsy was 96.83, 100 and 93.37 % respectively, which is quite comparable with other studies.

## 6. Conclusion

- Pulmonary cytology is an important, basic diagnostic tool for the detection of lung cancer, that too in early diagnosis.
- Fibroptic bronchoscopy is an easy , OPD procedure which is minimally invasive and without any risk. It provides

direct visualization of respiratory tract as well as lesion proper and variety of specimens can be collected.

- Imprint cytology is a rapid , reliable and inexpensive method , which does not require any extra procedure and provides an additional support to histologic examination.
- Technique of imprint cytology is simple , cost effective and rapid which appears more reliable than frozen section preparation, which requires more expertise trained persons for preparation and cost of maintenance of instrument as well.
- Combined use of bronchial brush, TBNA, imprint cytology and bronchial biopsy increases the accuracy and sensitivity of the diagnosis than use the single technique only.
- Imprint smears of trans-thoracic core biopsy helps to enhance diagnostic accuracy , whenever available.

## References

1. Agarwal, LH Ghotekar, RS Garbyal et al Evaluation of pulmonary malignancies in Kathmandu valley and role of bronchoscopic techniques in diagnosis of such cases, *Journal of Indian Academy of clinical medicine*, vol-4, No. 2, April June 2000 Pridjan G. Puschett JB. Preeclampsia. Part 1 clinical and pathophysiologic considerations. *Obstet Gynecol Surv* 2002; 57: 598 – 618.
2. Johnston WW, Elson CE. Respiratory tract. In: Bibbo M, editor, *Comprehensive cytopathology*. 2<sup>nd</sup> ed. Philadelphia: W.B. Saunders company; p. 325-401.
3. Parker SL, Tong T, Bolden S, Wingo PA : cancer statistics - 1997, *CA Cancer J. Clin*, 1997, 47 : 5-27.
4. Magrath I, Litvak J; cancer in developing countries opportunity and challenge. *J. Nat. Cancer, Irt*. 1993, 85(11) : 862-874.
5. US Department of Health and Human services A report of the surgeon General : The Health Benefits of Smoking cessation DHS pub. Nc (DC) 199-90-84t6.
6. Rosenow ES III : Neoplasm symposium on intrathoracic introduction *Myoclin Proc*. 1993, 68-168.
7. Travis W.D., Travis LD, devesa SS. Lung cancer, *Cancer*,. 1995; 75 : 191.
8. Ikeda B, Yanai N, Ishika S, Flexible fibre optic bronchoscope, *Keiro J. Med*. 1986, 17 : 1-16.
9. Pop D, Diagnostic sensitivity of different techniques in the diagnosis of lung tumors with the flexible fiberoptic bronchoscope. Comparison of brush biopsy, imprint cytology of forceps biopsy, and histology of forceps biopsy *Cancer* 1991, 67, 72-75.
10. S Agarwal, V.P. Mital, R. Chokhani et al role of bronchoscopic techniques in diagnosing of lung cancer, *Indian Journal of chest diseases*, 2000, Vol. 2.
11. A. Rosell, E. Monso, L. Lores et al. Cytology of bronchial biopsy rinse fluid to improve the diagnostic yield for lung cancer, *Eur Respir. j*. 1998; 12: 1415-1418.
12. W. Popp, H. Rauscher, L. Ritschka et al. Diagnostic sensitivity of different techniques in the diagnosis of lung tumours with the flexible fiberoptic bronchoscope, *Cancer*, 1991, 67 : 72-75.
13. R.R. Paulose, and I. A. Abdelhadi and Accuracy of touch imprint cytology in diagnosing lung cancer, *cytopathology*, 2004, Vol. 15, April.
14. L. Joos, N. Patato, P. Chhajed et al. Diagnostic yield of flexible fiberoptic bronchoscopy in current clinical practice; *Swiss Med. Wkly* 2006, 136 : 155-159.
15. Y. Adnana, U. Bahadyr, D. Sevim et al. Cell type accuracy of bronchoscopic biopsy specimens in primary lung cancer, *CHEST*, 1996, May pg 201-23.
16. M. Matsuda, T. Horari, S. Nakamura et al. Bronchial brushing and bronchial biopsy. Comparison of diagnostic accuracy and cell typing reliability in lung cancer; *Thorax*, 1986, Vol. 41, 475-478.
17. Govert J.A., Dodd L.G., Kussin P.S. A. Prospective comparison of fiberoptic transbronchial needle aspiration and bronchial biopsy for bronchoscopically visible lung carcinoma. *Cancer*, 1999, Vol. 87, No. 3, pg. 29-134.