



## Original Research Article

## Comparative study of bronchial brush and bronchial wash cytology in the diagnosis of lung tumors

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## ARTICLE INFO

## Article history:

Received 17-12-2020

Accepted 16-01-2021

Available online 10-03-2021

## Keywords:

Bronchial brush

Bronchial wash

Lung tumors

## ABSTRACT

**Context:** Cytological techniques are used as first line diagnostic tool in suspected lung tumors, based on which crucial management decisions are made. Bronchial brush (BB) and bronchial wash (BW) are two commonly employed techniques with variable diagnostic yield. This study compared the efficacy of BB and BW in diagnosing lung tumors.

**Aims:** To study sensitivity of BW and BB cytology in diagnosing lung tumours by correlating with biopsy as gold standard. To study the efficacy of BW and BB in typing the lung tumors.

**Methods and Material:** A cross sectional observation study for a period of 5 years was done. A total of 176 cases, suspected of lung cancer between January 2015 and December 2019 were selected, where cytology samples of BB or BW or both along with biopsy were obtained. Sensitivity, specificity, accuracy, positive predictive value and negative predictive value were calculated separately for BB and BW.

**Statistical analysis used:** All data were analyzed using SPSS software version 20.

**Results:** Sensitivity of BB was significantly higher (77.8%) when compared to BW (51.9%), while specificity was better for BW (90.9%) compared to BB (80%). Positive predictive value of BW was higher (97.6%) compared to BB (93.3%). Negative Predictive value of BB and BW was 50% and 21.3% respectively. BB showed better accuracy (78.3%) compared to BW (56.85).

**Conclusions:** BB is a much superior technique in diagnosing lung tumors, as it demonstrates far better sensitivity and accuracy. However, since specificity is higher with BW, both techniques should be concurrently used to obtain maximum diagnostic yield. BB has better efficacy in typing squamous cell carcinoma followed by small cell carcinoma and adenocarcinoma while BW is superior in typing small cell carcinoma followed by squamous cell carcinoma and adenocarcinoma

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### 1. Introduction

Lung tumor is most prevalent and also leading cause of cancer deaths worldwide.<sup>1</sup> Bronchogenic carcinoma was considered infrequent in India, previously. But in recent past, rise in trend in its incidence has been noticed. Lung cancer has been estimated to be most frequent among all newly diagnosed cases of malignancy in males and is emerging as an important cause of cancer deaths in females as well.<sup>1</sup>

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Prognosis of lung cancer is strongly related with stage of cancer at the time of diagnosis. 5 year survival rate ranges from 5% for IV stage and 80% for stage I cancers.<sup>1</sup> So early diagnosis is essential for improving prognosis of lung cancer. The only hope of combating the disease successfully remains in diagnosing the disease at the earliest possible stage.<sup>2</sup> Procedures used to diagnose lung tumors should be accurate as far as possible and should provide optimal characterization of tumor type. Endoscopic examination of tracheobronchial tree is the most proven valuable method in diagnosing lung cancer.<sup>3</sup> Its advent revolutionized

respiratory cytology as techniques like bronchial brush (BB), bronchial wash (BW), bronchoalveolar lavage and bronchial biopsy became more easy, accessible and popular.<sup>4</sup> Cytological diagnosis of respiratory samples obtained by flexible fiberoptic bronchoscope is the most commonly used technique and are safer, economical and provide quick results. Both BW and BB used concurrently are effective in diagnosis of lung tumor as it preserves both cells and architectural arrangement. Best result can be obtained by combining these techniques with radiological and histological findings.<sup>5</sup>

The availability of a reliable cytological investigative tool will enable us to diagnose lung cancer at an early stage making it amenable to treatment regimes which will ultimately affect patient's survival. Aim of the study was to compare the efficacy of BW and BB cytology in diagnosing and typing lung tumors.

## 2. Materials and Methods

This cross sectional observation study was conducted in a tertiary care centre. All patients who had clinical suspicion of lung cancer from January 2015 to December 2019 for a duration of 5 years were included.

### 2.1. Inclusion criteria

Patients with clinical suspicion of lung cancer who underwent flexible fiberoptic bronchoscopy for collection of cytological specimen and bronchial biopsy were included. Cases in which bronchoscopy showed abnormal appearance, suspicious of malignancy were included. All cases in which bronchial biopsy were received along with either BW or BB or both were included.

### 2.2. Exclusion criteria

For both cytology and histology, inadequate or unsatisfactory smears were excluded. Inadequate were those which showed poor cellularity, degenerated cells, necrotic debris or too much blood. Those cases in which cytological specimens were received without biopsy were not included.

Bronchoscopy and sample collection were done in Department of Respiratory Medicine, by the Pulmonologist. BB were obtained by cytobrush. Material was smeared on to minimum of 4 clean glass slides and immediately fixed in 80% isopropyl alcohol. Staining was done by Hematoxylin-Eosin (H&E) and Papanicolaou technique. One air dried smear was studied with Giemsa stain. BW was obtained from bronchial tree by instilling 20-30ml of isotonic saline and retrieving it. The fluid was collected in sterile 40ml container, centrifuged at 1500 rpm for 5-10 minutes. Minimum of 4 slides were prepared from cell sediment and fixed in 80% isopropyl alcohol. Staining was done by H&E and Papanicolaou technique. One air dried

smear was taken for Giemsa stain. Bronchial biopsy was taken in all cases during bronchoscopy and was fixed in 10% formalin. It was processed in automatic tissue processor Leica TP 1020 for 16-18 hours. Later, paraffin embedded blocks prepared and sections of 3-4 microns taken with the help of manual rotary microtome Leica RM 2245. Staining was done with H&E. Histopathological result was taken as diagnostic reference.

Cytological smears were categorised into malignant, dysplastic or atypical, inflammatory, no significant pathology. Malignant cells were further classified as squamous cell carcinoma (SCC), adenocarcinoma (AC), small cell carcinoma (SCLC) and poorly differentiated carcinoma. Biopsy specimens were grouped into malignant and inflammatory. Malignancy were further typed as SCC, AC, SCLC according to WHO 4<sup>th</sup> edition. Non Small cell Carcinoma which were difficult to categorize further based on morphology were classified as poorly differentiated carcinoma.

Sensitivity, specificity, accuracy, positive predictive value and negative predictive value were calculated for BB and BW in diagnosing lung tumors. All data were analyzed using Statistical Programme for Social Science (SPSS version 20). True positives (TP) were those cases which were cytologically and histologically malignant. All dysplastic/ atypical cases which later on proved malignant by biopsy were also included in this category. True negatives (TN) were cases which were not malignant on cytology and histology. Any case with a malignant/ dysplastic cytodiagnosis which was not malignant on histopathology was labelled as false positive (FP). False negative (FN) was a case which was not malignant on cytology, but later on biopsy turned out to be malignant. Sensitivity was the percentage of cases in which biopsy proved cancer cases were rightly diagnosed by cytology. Specificity was percentage of cases that were not malignant on biopsy which were correctly diagnosed negative on cytology. Accuracy means fraction of patients whose conditions were correctly diagnosed by cytology.

## 3. Results

The study included 176 patients with endobronchial lesions and high clinical suspicion of lung carcinoma. 154 were ultimately given a diagnosis of lung carcinoma confirmed by biopsy. Mean age of patients with lung cancer is 62.65 years ranging from 39 to 86. Peak incidence was found in age group 61–70 years, 62/154 cases (40.3%), followed by age group 51 – 60 years 22/154 (28.6%) and 24/154 cases (15.6%) in 7th decade. Lesser number of cases occurred before 40 years 2/154 cases and after 80 years 4/154 cases. Out of total 154 cases of lung cancer 96.1% were males (148 cases) and 3.9% were females (6 cases). Male to female ratio was 24.6:1. Cough with expectoration and hemoptysis were most common symptoms followed by dyspnoea, chest

pain and weight loss.

According to bronchoscopist's report, majority (126/176 cases) of patients had intraluminal growth with luminal narrowing, accounting for 71.6%. Extraluminal compression with mucosal infiltration was noted in 30/176 cases (17%). Non specific findings like ulcerative lesion or white patch or mucosal irregularity was seen in very few patients 20/176(11.3%). 65.1% of intraluminal growth was shown by SCC and 12.7% by SCLC where as extraluminal compression with infiltration was constituted mainly by AC (33.3%) and poorly differentiated carcinoma (20%) as confirmed by biopsy. Non neoplastic conditions showed non specific bronchoscopic findings including white patch or mucosal irregularity or ulcerated lesion

Histological cell types (Bronchial biopsy diagnosis for comparison as gold standard) were as follows- 92/176 cases (52.3%) SCC; 30/176 cases (17%) AC; 18/176 cases (10.2%) SCLC;14/176cases (8%) poorly differentiated carcinoma and non neoplastic lesions constituted 22/176 cases (12.5%)

BW result showed predominantly non neoplastic cytologic diagnosis 94/176 (53.4%). Among lung cancers, SCC constituted 32/176 (18.2%), SCLC10/176(5.7%), AC 8/176(4.5%) and poorly differentiated carcinoma constituted 2/176 (1.1%). 30/176(17%) cases showed dysplastic cells and could not be classified to specific tumour type due to few cells.[Table 1] Out of 92 BB specimens obtained, 30/92(32.6%) of BB were non neoplastic. Out of malignant cases diagnosed by BB, SCC constituted 26/92(28.3%) followed by AC 10/92(10.9%) and SCLC 6/92 (6.5%). Those cases which showed dysplastic cells and not typed comprised 20/92 (21.7%).[Table 2]

BW detected 80 malignant cases out of 154 biopsy confirmed cases. Thus TP was 80. FN cases were high, constituted 74. FP was 2. TN constituted 20.BB cytology detected 56 cases of lung cancer from 72 cases of biopsy confirmed malignancies. Thus TP was 56. FP was 4, a little higher in BB compared to BW. However FN cases were only 16, very less compared to BW.

Sensitivity of BB was significantly higher (77.8%) when compared with BW (51.9%). But specificity on the other hand was higher for BW (90.9%) compared to BB (80%). Positive predictive value of BW was 97.6% compared to 93.3% obtained by BB. Negative predictive value of BB was 50% and of BW was 21.3%. Regarding accuracy, BB showed better result 78.3% compared to 56.8% with BW [Table 3].

In typing of lung tumors, BB detected 22 out of 32 cases while, BW correctly typed only 30 out of 92 cases.6 cases of SCC were diagnosed as dysplastic cells by BB and 22 cases were typed to this category by BW. Thus BB showed better sensitivity and accuracy regarding typing of SCC. BW detected 8 out of 30 cases of AC. 4 cases showed dysplastic

cells. While BB rightly typed 10 of 22 cases of AC and dysplastic cells seen in 12 cases. In AC BB showed higher sensitivity and accuracy than BW. BW typed 10 of 18 cases of SCLC and 6 of 12 cases by BB Thus in typing SCLC, BW seems to be slightly more sensitive than BB

BB showed maximum sensitivity and accuracy in typing SCC(61.1%), followed by SCLC (50%) and AC(45%).While BW showed highest sensitivity in typing SCLC(50%) followed by SCC(32.6%)and AC(27.7%).[Table 4]

**Table 1:** Diagnosis of BW

Wash Diagnosis	Number of cases	Percent
Non neoplastic	47	53.4
Squamous cell carcinoma	16	18.2
Adenocarcinoma	4	4.5
Small cell carcinoma	5	5.7
Poorly differentiated carcinoma	1	1.1
Dysplastic cells	15	17

BW- Bronchial wash

**Table 2:** Diagnosis of BB

Brush Diagnosis	No of cases	Percent
Non neoplastic	15	32.6
Squamous cell carcinoma	13	28.3
Adenocarcinoma	5	10.9
Small cell carcinoma	3	6.2
Dysplastic cells	10	21.7

BB- Bronchial brush

**Table 3:** Diagnostic role of BW and BB in lung tumors

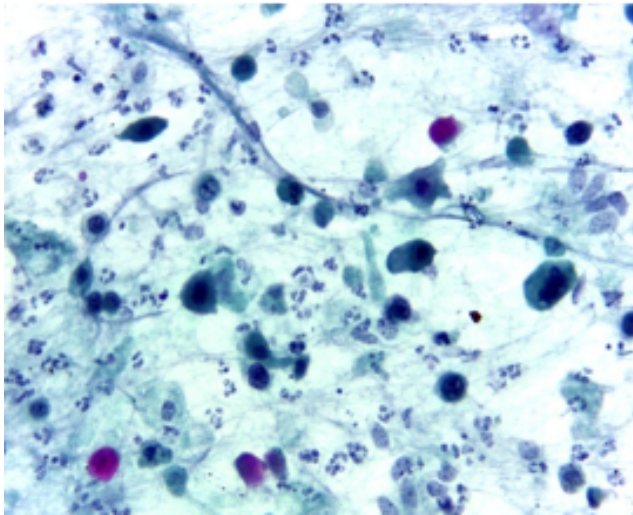
	BW	BB
Sensitivity	51.9	77.8
Specificity	90.9	80.0
Positive Predictive value	97.6	93.3
Negative Predictive value	21.3	50.0
Accuracy	56.8	78.3

BW- Bronchial wash, BB- Bronchial brush

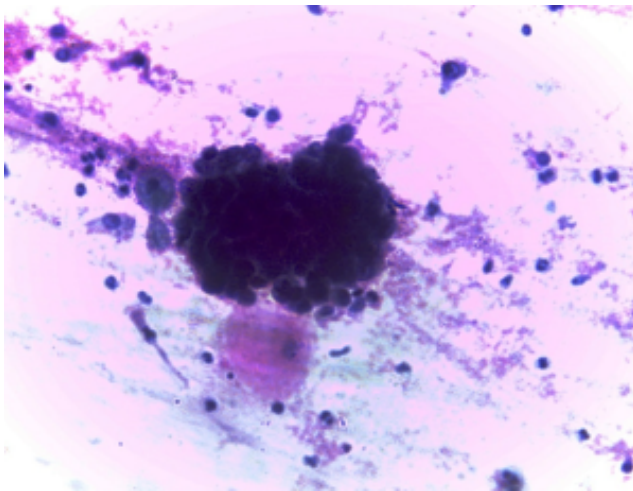
**Table 4:** Role of BW and BB in typing lung tumors

	SCC		AC		SCLC	
	BW	BB	BW	BB	BW	BB
Sensitivity	32.6	61.1	27.7	45	55.6	50
Accuracy	31.9	55.0	27.7	45	55.6	50

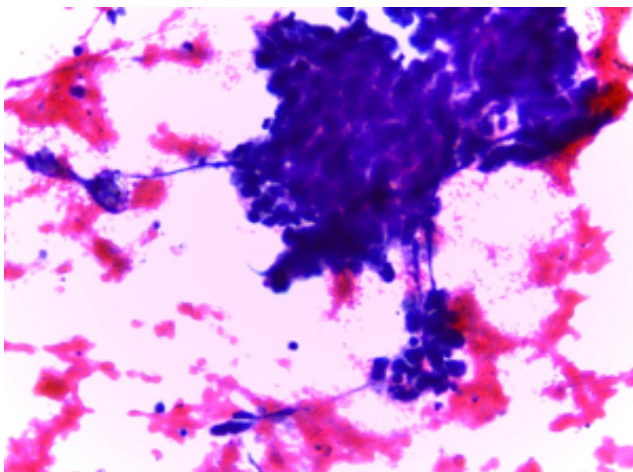
BW- Bronchial wash, BB- Bronchial brush, SCC- Squamous cell carcinoma, AC-Adenocarcinoma, SCLC-Small cell carcinoma



**Fig. 1:** Bronchial wash of Squamous cell carcinoma



**Fig. 2:** Bronchial brush of Adenocarcinoma



**Fig. 3:** Bronchial wash of Small cell lung carcinoma

#### 4. Discussion

With the advent of fiberoptic bronchoscopy, respiratory cytology took a new turn as cytological samples like BB and BW could be collected from respiratory tract, yielding significant amount of cytologic material. This study mainly assessed diagnostic value of BB and BW cytology in detecting lung cancer in comparison to corresponding histological diagnosis in patients with suspicious lung cancer who underwent fiberoptic bronchoscopy.

Majority of lung cancer patients in this study belonged to 5<sup>th</sup> and 6<sup>th</sup> decades (68.9%) with mean age of 62.65 years. This is in concordance with the literature. 96.1% of lung tumors occurred in males compared to 3.9% in females, with M:F ratio of 24.6:1, which is higher compared to other studies. This may be attributed to habitual smoking in males compared to females. The common symptoms of presentation are cough with expectoration, hemoptysis and dyspnoea. A few cases presented with chest pain, associated weight loss and anorexia.

In regard to bronchoscopic appearance in current study, majority of intraluminal proliferative growth are SCC and SCLC, whereas extraluminal compression with infiltration pattern was constituted mainly by AC and poorly differentiated carcinoma. These findings are in agreement with Butnor et al and Buccheri et al.<sup>6,7</sup> Butnor et al observed, majority of adenocarcinoma were causing external compression.<sup>6</sup>

In present study, BB could detect malignancy in 56 out of 72 malignant cases and found to have a sensitivity of 77.8% and specificity of 80%. This finding is similar to result which was observed by Bodh A et al and Rateesh S et al.<sup>2,8</sup> Both researchers obtained sensitivity of BB as 77.78. Shagufta TM et al obtained sensitivity of BB as 82.1% which is higher compared to current study.<sup>9</sup>

BW has been able to diagnose of 80 out of 154 malignant cases in present study. The sensitivity of BW is 51.9% and specificity 90.9%. There has been a controversy as to whether BW should be routinely used or not. Previous studies by Chaudhury M et al and Rawat J et al found comparable result of BW in lung cancer cases.<sup>10,11</sup> However Lee GD et al and Shagufta TM et al obtained good diagnostic yield with BW which was at variance with this study.<sup>9,12</sup>

In current study, in comparison to BW, BB gave a higher number of TP and TN and lesser number of FN cases, showing superiority of BB over BW. High percentage of FN with BW could be because of BW technique relies mainly on cells exfoliated from malignant lesion in bronchial epithelium and the adequacy of its samples depend on several factors especially preservation of morphology of cytological material obtained, degree of differentiation of malignant growth and technical skill of pulmonologist in performing washing in retrieving wash fluid.<sup>13</sup>

In general poorly differentiated lesions have more loosely cohesive cells in comparison with well differentiated malignancies.<sup>14</sup> Such lesions exfoliate larger number of cells than well differentiated carcinoma. Secondly, exfoliated cells undergo degeneration while lying in bronchus, thus losing morphological integrity which are important in distinguishing them from normal exfoliated cells from bronchial epithelial lining. Regarding the technical skill of pulmonologist, adequacy of cytologic material depends on amount of wash fluid retrieved from bronchus. If this is less, it may result in FN result. All these factors affect the overall diagnostic yield of BW specimens.

BB technique has the advantage that the surface of suspicious lesion is scraped by brush passed through bronchoscope. The cells get dislodged from surface of well differentiated malignant lesions too which do not exfoliate cells readily. Thus chances of getting adequate diagnostic material by BB is greatly increased, compared to BW technique. Moreover, the retrieved cells show better preserved morphology compared to cells that have already exfoliated to bronchial cavity.

#### 4.1. Typing of tumour

The precise sub classification of lung tumors is critical for the effective management of patients.<sup>15</sup> A false classification will lead to delayed treatment and high mortality. This is specifically applicable for advanced lung cancer patients with unresectable disease. In current study BW and BB cytology in tumor typing was evaluated in comparison to biopsy, considering cell type diagnosed from biopsy material will be an accurate reflection of tumor type.

In the present study BB could diagnose 61.6% of the cases as SCC. Next higher typing accuracy was with SCLC in which BB diagnosed 50% of cases. Similarly 45% of AC cases were rightly diagnosed by BB. While BW was able to morphologically diagnose only 32.6% of SCC cases and 27.7% cases of AC. BW showed highest typing accuracy with SCLC that is 55.6%.

Thus it has been observed that samples obtained by BB showed better cytological detail than BW which helped in specific morphological classification of lung cancer especially in SCC and AC. However typing of SCLC is better with BW (55.6%) compared to BB (50%). There is only subtle difference in accuracy between the two techniques in typing SCLC.

The diagnostic value of BB was highest in those with SCC followed by SCLC. This finding implies that BB cytology is beneficial to the diagnosis of SCC and SCLC compared to AC and poorly differentiated carcinoma. Similarly, better typing of SCC and SCLC were observed by other investigators like Troung et al, Hsu C et al and Payne CR et al.<sup>16–18</sup> Better typing in SCC and SCLC may be due to central location of these tumors. Hence it is easy to obtain a great number of tumor cells with BB. In contrast,

AC is generally located in peripheral portion of lung and it is more difficult to obtain sufficient number of tumor cells.

Typing difficulty arises due to various reasons. Metaplastic squamous cells in AC may be wrongly interpreted as SCC and conversely in SCC, the cells may be clustered with large nuclei suggesting AC. Moreover, loosely coherent, pleomorphic cells of large cell carcinoma and cells shed by polygonal SCLC can be mistaken for SCC.

Cytological diagnosis of Dysplastic cells for SCC and AC is given due to presence of few abnormal cells and absence of pattern to categorize further. Good number of samples of BW (36%) and BB (32%) were classified as positive for dysplastic cells. However overall results show BB as better technique compared to BW in morphological classification of malignant samples. Follow up and repeated cytological and histopathological study will be required in these cases. One of the limitations of this study is the use of very small bronchial biopsy specimen for the validation of cytological techniques and absence of other confirmative tests like surgical biopsy, biopsies of extrapulmonary metastatic lesions and autopsy.

To conclude BB is a much superior technique in diagnosis and morphological typing of lung cancer, as it demonstrates far better sensitivity and accuracy, in comparison to BW. However, since specificity is higher with BW, both techniques should be concurrently used along with biopsy to obtain maximum diagnostic yield. Morphologic typing of cytologic techniques are better in central tumours (SCC and SCLC), compared to peripheral tumours (AC).

#### 5. Acknowledgement

I would like to thank the faculty, my colleagues and technical staff of Department of Pathology, MES medical college, Perinthalmanna for helping and guiding me through this work

#### 6. Source of Funding

No financial support was received for the work within this manuscript.

#### 7. Conflict of Interest

The authors declare that they have no conflict of interest.

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**Cite this article:** Zainudeen F, Nair LK, Suhail N, Jayalakshmy P.S, Sideeque N A. Comparative study of bronchial brush and bronchial wash cytology in the diagnosis of lung tumors. *IP J Diagn Pathol Oncol* 2021;6(1):9-14.