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# Role of I-scan technique in screening for lung cancer in smokers with positive sputum cytology

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## Abstract

**Background:** Lung cancer has a very poor prognosis and high mortality. Positive sputum for malignant and/or atypical cells warrants the need for fiberoptic bronchoscopy. White light bronchoscopy (WLB) is usually unable to detect preinvasive lesions; therefore, autofluorescence bronchoscopy (AFB) was introduced as a gold standard for detecting such lesions. The aim of this work was to investigate the role of I-scan as a screening tool for cancer in smoker patients showing positive sputum cytology.

**Results:** New suspicious findings under I-scan occurred in 11 patients (36.7%). The overall sensitivity of WLB alone to diagnose malignancy is 23.3%, in contrast to an added sensitivity of 50% when I-scan was combined with white light ( $p$  value < 0.05). The specificity of I-scan could not be assessed in the absence of control cases (true negatives). No major complications or deaths occurred. Haemorrhage and bronchospasm were the commonest minor complications.

**Conclusions:** The addition of I-scan to the routine white light examination can increase the overall sensitivity of bronchoscopic screening in cases of sputum suspicious for malignancy if put in experienced hand. The suggested increase in procedure duration due to the combined use of I-scan and white light bronchoscopy is not associated with life-threatening complications.

**Keywords:** Lung cancer, Sputum cytology, Bronchoscopy

## Background

Lung cancer has less than 15% 5-year survival rates with a mortality rate of more than 90% [1]. Despite the early negative recommendations of the United States Preventive Services Task Force (USPSTF) against screening for lung cancer in both 1985 and 1996 [1], the new published screening studies changed the USPSTF recommendations in 2013 to be grade “B” for annual screening with low-dose computed tomography (LDCT) [2].

Positive sputum for malignant and/or atypical cells, especially in risk group patients, is likely an indicator for the need for fiberoptic bronchoscopy to confirm

malignancy with a hope of curable resection [3]. White light bronchoscopy (WLB) is usually unable to detect preinvasive lesions; therefore, autofluorescence bronchoscopy (AFB) was introduced as a gold standard for detecting such lesions [4–6]. I-scan technology is a novel endoscopic imaging technique based on a digital contrast process involving three modes of image enhancement: surface enhancement, contrast enhancement and tone enhancement [7, 8]. In contrast to AFB, I-scan depends on the use of one light source giving full-spectrum white light followed by image enhancement on real-time basis, which is easier and more convenient [9].

## Methods

In this non-controlled prospective interventional study, we recruited 143 patients between September 2018 and

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till July 2019, with the inclusion criteria of being a current or former smoker and aged 45 years old or more. Patients with any suspicious lung shadow or infiltrate on plain chest radiographs and CT, in addition to those having any contraindication to bronchoscopy procedure (e.g. recent cardiac events, non-corrected hypoxaemia and severe bleeding disorders), were excluded. In all procedures, we strictly followed the faculty ethics committee standards and a written informed consent was taken from each patient.

We took a representative sputum sample (confirmed by the presence of alveolar macrophages or bronchial epithelial cells [3], which if absent, samples were recollected) from each patient and subjected to cytologic examination for atypical or suspicious cells. Some of each sputum sample was crushed on a clean glass slide by another slide in a rotary pattern. Then, the material was distributed evenly over the slide by making overlapping horizontal strokes producing a smear only slightly thicker than that of the blood. For Papanicolaou stain, slides were fixed immediately in 95% ethyl alcohol, while for May-Grunwald stain, slides were air-dried and fixed in 100% methanol.

After inclusion of 30 patients with positive sputum cytology, recruitment was stopped and all positive patients were subjected to endoscopic examination of whole accessible part of the bronchial tree by high-definition white light bronchoscopy then I-scan mode (using Pentax™ videobronchoscope; Pentax EPK-i5000 High-Definition Video Processor, and Pentax EB-1990i HD+ Bronchoscope) [9, 30]. All suspicious bronchoscopic findings were reported first under high-definition white light (HD/WLB) then under I-scan modes, starting with I-scan 1, then I-scan 2 and lastly I-scan 3, applying the default factory settings for each mode.

“De novo” inspected lesions under any of the I-scan modes, which were not initially noticed under high-definition white light, were clearly reported. Biopsies were taken as indicated using forceps, brush and/or needle with a minimum of five samples [10]. Besides, bronchoalveolar washings by injecting at least 100–120 mL of sterile saline [11] were taken.

Monitoring was continued after the procedure for possible complications which may be major life-threatening (cardiorespiratory arrest, respiratory failure requiring mechanical ventilation, shock, pneumonia, pneumothorax, arrhythmias and pulmonary oedema) or minor non-life-threatening (vasovagal reactions, laryngospasm, bronchospasms, fever, haemorrhage, nausea and vomiting).

Obtained samples were sent for histopathological and cytological analysis where the pathologist was blind to mode under which biopsy was taken. Pathological results of all sent samples were recorded and categorized as positive or negative for malignancy, and then this was

followed by making correlations between pathological yield and the mode under which each biopsy was taken and statistical analysis of all obtained data using the chi-squared test for independence to detect statistically significant difference in sensitivity of each bronchoscopic mode to diagnose malignancy, available at <https://www.socscistatistics.com/tests/chisquare2/default2.aspx>. Study flow chart is shown in Fig. 1.

## Results

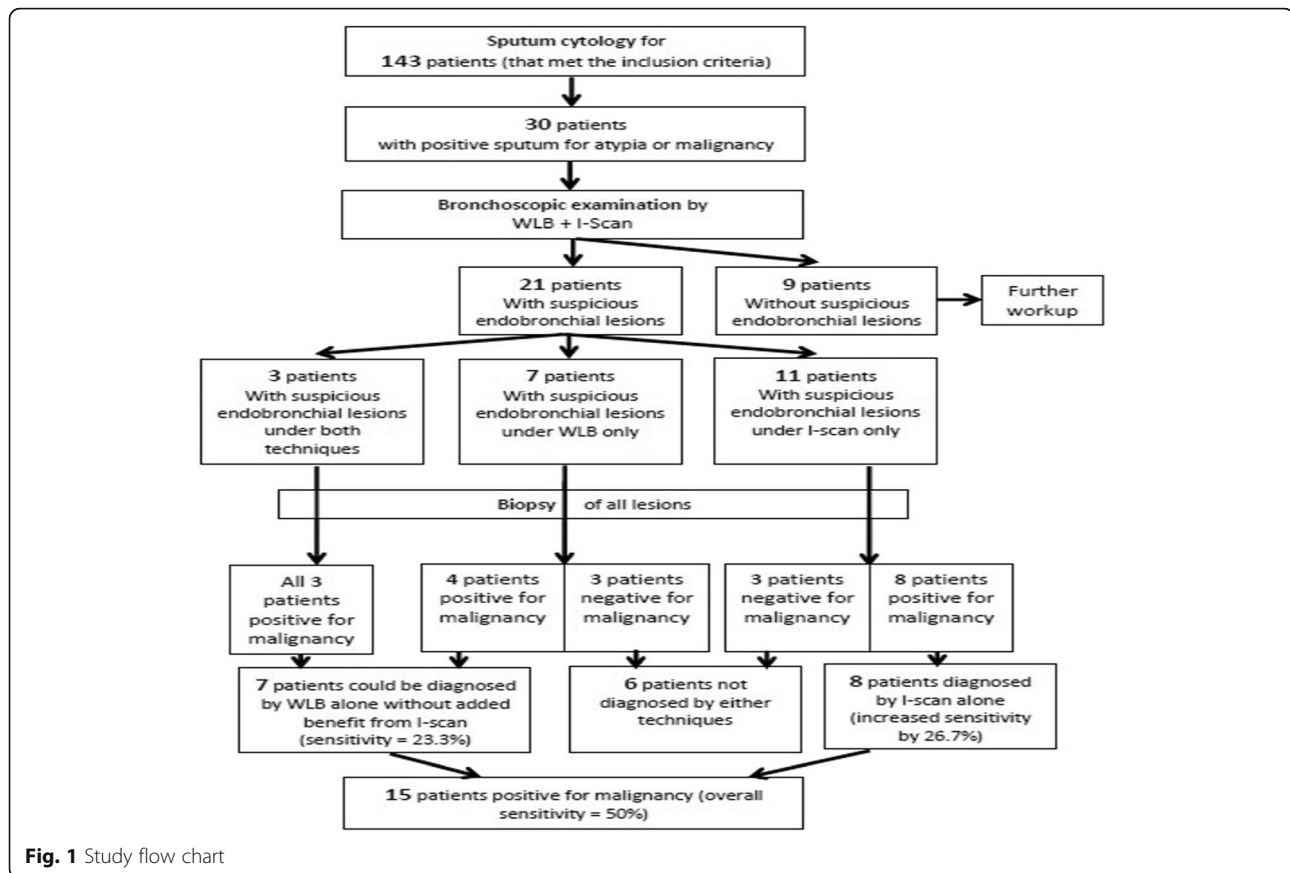
Demographics of the study population are grouped in Table 1. Significant endobronchial findings, suspicious for malignancy, were visualized in 21 patients (70%). I-scan showed “de novo” endoscopic suspicious lesions, which were not noticed initially under WLB, in 11 patients, i.e. 36.7% of the study cohort (Fig. 2). The addition of I-scan to WLB gave a significantly higher number of positive endobronchial results (the chi-squared test for independence result was 8.0756. The  $p$  value is 0.004486, so this is significant at  $p < 0.05$ ).

None of the major complications occurred in any of the patients. The only two minor complications that we encountered were haemorrhage (11 patients, 36%) and bronchospasm (4 patients, 13%); however, both were self-limited and had no any clinical significance. No mortalities were found in our study.

Fifty percent of cases (15 patients) showed positive results for malignancy. The distribution of positive pathological results according to histological type is shown in Table 2. Biopsies taken under WLB (without new lesions to be biopsied under I-scan) were positive in 4 patients, in addition to another 3 patients that showed positive results in biopsies taken from both endoscopic lesions seen under both bronchoscopic techniques. Thus, WLB could diagnose all the 7 patients without added benefit from I-scan. Meanwhile, I-scan succeeded to give additional positive results in 8 patients (Fig. 1). Thus, the overall sensitivity of WLB alone is 23.3%, in contrast to an added sensitivity of 50% when I-scan was combined with white light (the chi-square test for independence result was 4.5933; the  $p$  value is 0.032097, so this is significant at  $p < 0.05$ ). The specificity of I-scan could not be assessed in the absence of control cases (true negatives).

## Discussion

Many, relatively old, studies have shown a wide range of sensitivities of sputum cytology screening for atypical and/or malignant cells in different study populations with different risks and exposures. Positive results were ranging down to 40% in peripheral tumours and up to 90% in more central cancers [12–26]. We found positive sputum results in 21% of our recruited patients. We could not report our sensitivity rate due to the absence



of false negative cases in the absence of a follow-up of sputum negative cases.

Lam et al. studied 181 high-risk patients and detected atypia in 47% of them. Positive cases underwent bronchoscopy and CT scans of the chest with consequent diagnosis of primary lung cancer in 15% of these patients, and almost half of them were at stage I or II. Sputum cytology sensitivity for lung cancer detection was 71% for all histologic types and 100% for squamous cell carcinoma [27]. Because of the “short follow-up” nature of our study, we cannot accurately compare our results to those of the latter study. However, in the same context, we can appreciate that nearly half of our patients

who proved to be malignant were of squamous cell type (47%). Obviously, this can be easily anticipated due to the “centrally located” nature of squamous cell carcinomas. In 1985, Risse et al. reported that cytologic typing accuracy was 67% for large cell carcinomas, 73% for adenocarcinomas, 91% for small cell lung cancers and 98% for squamous cell carcinomas. In addition, they pointed to another very important factor to be considered when talking about sputum cytology sensitivity as they concluded that in patients with primary lung cancer, the proportion of correct positive diagnoses increased from 0.47 to 0.87 with one to five sputum specimens examined [28]. We collected and analysed just one sample of sputum from our study patients as this was just a preparatory step before going to the main focus of our research, namely, I-Scan bronchoscopy.

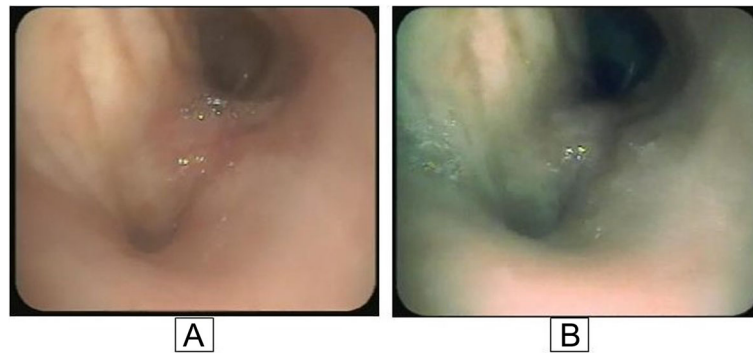
Bronchoscopic imaging techniques, such as AFB or narrow-band imaging (NBI), facilitate the detection of premalignant lesions and early lung cancer [7, 29]. However, the majority of lung cancer patients are diagnosed in an advanced stage. I-scan, which is an image-digital processing technique, succeeded in the detection of new suspicious endoscopic findings in 67.5% of the patients with a radiologically evident lung mass. Van der Heijden et al. in 2015 did not report significant differences in the

**Table 1** Demographic data of the studied cases

Age (years)	61 ± 9
Gender	Male, 22 (73.3%) Females, 8 (26.7%)
Smoking status	Current, 17 (56.7%) Former*, 13 (43.3%)
Environmental/occupational exposures <sup>†</sup>	Yes, 25 (83.3%) No, 5 (16.7%)

\*Stopped smoking for 6 months or more

<sup>†</sup>Any established offending exposures for the development of lung cancer



**Fig. 2** a WLB of apparently just thickened right main stem spur. b I-scan 3 showing infiltrated spur by a nodular mass

average number of tumour sites detected per patient under WLB, HD/WLB, AFB or I-scan modes [9]. While in 2018, the same research group in addition to other investigators from another four centres reported that additional lesions were detected with I-scan in one-third of all patients and 22% of these lesions had a clinical relevant pathology outcome, potentially influencing treatment [30].

For a closely related bronchoscopic modality which is AFB, many studies showed that it increased the sensitivity to diagnose moderate-to-severe dysplasia from 9 to 65% and for CIS, this reached up to 100%. However, AFB did not gain much popularity in daily practice. This may be explained by the decreasing prevalence of central tumours, in combination with the need for a specifically wave-lengthed light source (390–440 nm) [4–6, 31–42]. Therefore, the results of the published series did not support its general routine use as a diagnostic tool for lung cancer [43].

For another commonly addressed bronchoscopic technique in the field of lung cancer screening which is NBI, a relatively recent meta-analysis published in 2017 and based on four studies found that the pooled sensitivity of NBI to detect lung cancer was 91% (both CIS and invasive lesions) compared to a pooled sensitivity of WLB of 70% [44–48]. In one of these four studies, Herth et al. compared AFB and NBI in the detection of intra-epithelial neoplasia. Both techniques were more sensitive than WLB alone (3.7 and 3.0 times, respectively). However, there was not a significant diagnostic value of combining AFB and NBI together [45]. The commonest histological type that we encountered was squamous cell

carcinoma. This may be attributed to the nature of these tumours being more central than other types, and this finding matches many other similar studies; one of the closest was that conducted at the bronchoscopy unit in Abbasia Chest Hospital [49].

Obviously, this presenting study has some limitations. A larger number of cases would give more reliable and reproducible results. A direct comparison of I-scan with other common image processing devices (especially, AFB and NBI) would be very beneficial in terms of drawing conclusions about relative sensitivity and specificity of each technique. Unfortunately, the non-availability of these devices in our department prevented this valuable comparison. The inability to follow up the sputum negative cases hindered the final conclusion for the sensitivity of I-scan.

## Conclusion

From all previously mentioned, we can conclude that the addition of I-scan to the routine white light examination can increase overall sensitivity of bronchoscopic screening for lung cancer in smoker patients with positive sputum for malignancy. If put in experienced hand, the suggested increase in procedure duration due to combined use of I-scan and white light bronchoscopy does not lead to major complications or deaths. Minor complications like bleeding and bronchospasm are common in bronchoscopy procedures, but they are usually tolerated and are not associated with significant adverse events.

## Abbreviations

USPSTF: United States Preventive Services Task Force; LDCT: Low-dose computed tomography; WLB: White light bronchoscopy; AFB: Autofluorescence bronchoscopy; CT: Computed tomography; HD/WLB: High-definition white light bronchoscopy; NSCLC: Non-small cell lung cancer; SCLC: Small cell lung cancer; NBI: Narrow-band imaging; CIS: Carcinoma in situ

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Not applicable

**Table 2** Diagnosed histopathological types

Squamous cell carcinoma	7 (46.7%)
Adenocarcinoma	3 (20%)
Poorly differentiated NSCC	2 (13.3%)
SCC	3 (20%)

The total number of cases with positive biopsies for malignancy was 15  
NSCLC non-small cell lung cancer, SCLC small cell lung cancer

**Authors' contributions**

AA collected the sputum samples, performed the bronchoscopy procedure, analysed and interpreted the data and was the major contributor in writing the manuscript. DA performed the cytological examination of the sputum and the histological examination of biopsies. The authors read and approved the final manuscript.

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**Availability of data and materials**

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

**Ethics approval and consent to participate**

Alexandria medicine faculty ethics committee (IRB NO: 00007555-FWA NO: 00018699) approved this research on 12 April 2018 with a serial number of 0303912. A written informed consent was taken from each patient.

**Consent for publication**

Not applicable

**Competing interests**

The authors declare that they have no competing interests.

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