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Guidance in Assisting the Identification / Interpretation of Lung Cancer using Bronchoscope

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Abstract— Lung Cancer is one of the leading disease in the world, and increased in many countries. The eight year overall survival rate is just 17%. We have to remove lung cancer surgically at an early stage to ensure the survival of the patient. There are several methods to treat an early staged lung cancer such as Brachytherapy, Cryotherapy, Photodynamic therapy, Argon plasma cogulation, Thermal laser, micro debrider, electrocautery etc. In this review we are going to discuss various types of bronchoscopy and their positive and negative sides.

Keywords— Lung cancer, bronchoscopy

I. INTRODUCTION

The first sign of evolution of bronchoscope was apparent when a German physician, Gustav killian removed a pork bone from the right main bronchus of a Black forest worker in the year 1897. He had used a similar device with the same limitations as that of a modern bronchoscope includes two types of devices – rigid and flexible each having their own positives and negatives.

II. CHOOSING BRONCHOSCOPY

Bronchoscopic treatment is advisible for treating only lung cancer at an early stage. But bronchoscopy is a cost effective treatment. The patient undergoing treatment should not have low life expectancy. These are some criteria for choosing bronchoscopy. Let us decide which bronchoscopy to choose rigid or flexible. Rigid bronchoscopy is defined as trans oral or trans tracheosomy passage of rigid instruments for diagnosis or therapy aided by various light sources, telescopes and instruments , requiring a general anaesthetic.

Flexible bronchoscopy is defined as a technical procedure that is utilized to visualize the nasal passage from nasal opening to bronchial tree end which is usually carried out under conscious sedation.

Mostly a flexible bronchoscopy is preferable because a rigid brochoscopy requires a lot of skill. Majority of doctors in US and UK lack this skill. But there are some circumstances in which rigid bronchoscopy is advisable.

Unstable patients, those with significant underlying cardio pulmonary disease, uncontrolled coagulapathy and those with cervical instability need to be carefully assessed. Mortality from flexible bronchoscopy is rarer than with rigid bronchoscopy. Rigid bronchoscopy requires a skilled anaesthesiologist support.

A. Comparative study of different bronchoscopical methods

TABLE I

Types of bronchoscopy /characteristics	**Electrocautery**	**Argon Plasma Coagulation**	**Thermal laser**	**Microdebrider**	**Cryotherapy**	**Brachytherapy**	**Phtotodynamic therapy**
Indication	Hemoptysis, Debulking of endobronchial tumor	Hemoptysis, Debulking of endobronchial tumor	Debulking of endobronchial tumor	Debulking of endobronchial tumor	Debulking of endobronchial tumor	Treatment of endobronchial or peribronchial tumor	Treatment of endobronchial or peribronchial tumor
Effect	Immediate	Immediate	Immediate	Immediate	Delayed	Delayed	Delayed
Rigid or Flexible	Both	Both	Both	Rigid	Both	Both	Both
Caution and Contraindic-ation	Pace maker or defibrillators Fio_2 of > 0.4(burns)	Per Electrocautery	Fio_2<0.4 Contraindica-tion No exphytic lesion visible. Total airway obstruction and no functional distal airway open	None Distal lesion	None Acute airway Obstruction requiring immediate relief	Expensive Healthcare worker shielding Treatment for malignant tracheoeso-phageal fistula	Skin photosensitivity for several weeks Massive hemoptysis, Bronchopleural fistula, Subepithelial fibrosis

B. Advances in Therapy

Using Bronchoscopy (Immediate Effect)

1) *Electrocautery*: Electrocautery uses a high frequency electrical current which causes a heating of the tissues that the probe is with contact. Coagulation is achieved in low voltage and tissue will be vaporized in high voltages. The difficulties of endobronchial electrocautery include that of general bronchoscopy. Application of deep electrocautery too close to the bronchial well may result in perforation and pneunothromax.

Electrocautery is a safe, cheap and effective therapy for early stage and advanced cancer with MAO(Malignant Airway Obstruction).

2) *Argon Plasma Coagulation:* Argon Plasma Coagulation has to resect MAO and to control endobronchial bleeding . A beam of argon gas acts as a non contact for the electrocautery effect which distinguishes APC from electrocautery. APC is a cheap , safe and effective modality for treating both MAO and hemoptysis.

3) *Laser:* A Laser in bronchoscopy started almost thirty years ago. Bronchoscopic laser resection is a useful modality in the treatment of MAO. Airway obstruction to bronchogenic cascinoma is the most frequent indication for laser resection.The tumor is removed by two methods,

1. Resection
2. Vaporization

In the first one the laser is aimed at the target lesion and through photocoagulation of the feeding blood vessels and amelioration of the lesion the devitalized tissue is removed through the bronchoscope.

The second, which is vaporization involves aligning the laser parallel to the bronchial wall and aiming at the edge of the intraluminal lesion. Laser pulses have limits to 1s or less. The laser is used in parallel with the target lesion and not straight on or perpendicular to reduce the chances of perforation.

A Cheaper endobronchial laser is now a days available. [neodymium:yttrium-aluminum perovskite(Nd:YAP)] . One study of 133patients with various malignant and benign(7 patients) indications concluded that the Nd:YAP laser was a safe and effective tool for bronchoscopy.
Laser through bronchoscopy is an effective approach for treatment MAO. ND:YAG laser is expensive. It needs trained staff to operate with safety to prevent injury to patients.

4) Microdebridement:

A microdebridement operates by using a powered rotating blade and a simultaneously operating suction device to facilitate the removal of debris.

The elongated rotating tip microdebrider to about 45cm is the special and it is accurate and allows high flow oxygen. The comblications of thermal such as airway injury, airway fires, tracheoessophgeal fistuals can be avoided using micro debridement. The complications are hemorrhage, perforation and pneumothorax.

Delayed effect: (Cryotherapy)

In 1812 during Russian Campaign , cryotherapy is a cheap and effective treatment for many medical conditions. The bronchoscopic cryotherapy is a procedure where, either through rigid or flexible bronchoscopy, malignant or benign tissue is ablated by repeatedly freezing , thawing and refreezing. Cryotherapy may be considered for MAO in patients without critical airway narrowing . Main advantages is no limitation in oxygen delivery during the procedure.

Brachytherapy is an invasive two step technique. The first step is to identify the target lesion and the second step is to remotely under fluoroscopy and computer guidance. Place the radioactive source beside the target lesion and also changes in its position in a staged process to allow irradiation on the target lesion.

Irridium 192 is the most common isotope used because it permits a dramatic reduction of treatment time reduces costs, enhances the patient experience and allows for an outpatient setting over several sessions.

Lowdose Rate is less than 2Gy/h and max of 1500 – 5000cGy over 3 days. And costly cumbersome with radiation protection measures. HDR is about 12 Gy/h with the dose varying from 100 to 300 cGy. HDR is less costly than LDR and enhances the patient experience.

Brachytherapy is effective in the palliation of both endobronchial and peribronchial malignancy with a delayed effect. Significant risk of hemoptysis is found.

5) Photo dynamic Therapy:

Skin cancers can be treated by photodynamic therapy. This therapy has a successful record for malignant and benign conditions.

PDT has been combined with other endobronchial therapies, including brachytherapy therapies which are brachytherapy and laser therapy. Complication of PDT are sunburn upto 6 weeks post HPD administration is a concern and patients need to be fully informed to avoid sunlight and to wear appropriate clothing.

PDT is effective in debulking and palliation with delayed effect and no limitation of oxygenation in MAO.

C. . Airway stents

Tracheobronchial prostheses or Airway stents are tube shaped devices that are inserted into an airway to maintain airway patency. These are made of metal , silicone or other meterials can be used to relieve airway obstruction caused be malignant tumors.

Stent therapy is indicated in both intraluminal and extraluminal major airway obstructions.
After removal of endobronchial obstruction stents can be considered to maintain airway patency. Self expandable metal stents should not be placed in patients where removal is considered in future.

D. Techniques in Bronchoscopy

1). Genomic classifier for lung cancer by diagnostic bronchoscopy

Low Dose Computed Tomography (CT) screening results in a 20% relative mortality reduction in high risk[2]. The gene expression profile of cyto logically normal bronchial airway epithelial cells has been shown to be altered in patients with lung cancer. A gene expression classifier from airway epithelial cells that detects the presence of cancer in smokers. Bronchoscopy suspect lung cancer and evaluated its sensitivity to detect lung cancer among patients from an independent cohort. Bronchoscopy is considered to be safer than other invasive sampling methods such as transthoracic needle biopsy(TTNB) or surgical techniques[3].

Classifier development

Initially training data to select genes which were gender, tobacco use and smoking history to identify gene expression correlated of these clinical variables.

Lung Cancer – related genes were then selected and a classifier for predicting the likelihood of lung cancer based on the combination of the cancer genes, the gene expression correlates and patient age was derived. All aspects of this classifier development procedure were determined using cross validation and using only data from the training set samples.

A logistic regression model with lung cancer status (cancer positive = 1 and cancer negative = 0) as the dependent variable was fit using the training data clinical factor gene expression correlates and patient age as predictors. This severed as the baseline for subsequence gene analysis.

The classifier adds substantial sensitivity the bronchoscopy procedure resulting in high NPV. This can be used to aid in decision making when bronchoscopy is non diagnostic by identifying patients who are at low risk of having lung cancer. ROC curve analysis of the training set cohort using the finalized gene expression classifier is evaluated.

Classifier accuracy was measured by the area under the curve, sensitivity, specificity, NPV and PPV , cross validation using a 10% sample hold-out set[4].

TABLE III

Sensitivity of Bronchoscopy , the classifier and Combined procedures comparison by size

Mass size	**N**	**Bronchoscopy sensitivity**	**Classifier sensitivity**	**Combined sensitivity**
< 3 cm	99	44%	87%	93%
>3 cm	48	58%	94%	98%
Infiltrate	16	38%	100%	100%

2) Stem Cell – Associated Markers in human airway obtained via fiberoptic bronchoscopy

The cancer stem cell (CSC) theory proposes that tumors, which is cause for tumor growth, invasion and metastasis[1]. CSC and normal tissue stem cells share important things: self renewal, multipotency and unlimited proliferation, and potentially overlapping molecular mechanisms**.** The Chi-Square test and the Mann-whitney U test were applied to compare the expression of markers between mRNA expression markers and lung cancer clinical factors**.** Malignant transformation originate from adult stem cells and may thus express the stem cell associated markers. The purpose is to investigate the differential expression and clinical significance of seven stem cell associated markers (Bmi1,CD 133,CD 44, Sox 2, OCT 4 and MSi2) in lung cancer providing new targets for the diagnosis and treatment of lung cancer[10].

TABLE IIIII

Specificity, accuracy and sensitivity of seven stem cell associated markers mRNA in biopsy samples obtained from bronchoscopy

	Specificity %	**Accuracy %**	**Sensitivity %**
Bmi 1	33.3	80.8	88.4
CD133	44.4	80	85.7
CD44	11.1	86.2	98.2
Sox2	16.7	86.9	98.2
Nanog	66.7	63.8	63.4

OCT4	61.2	82.3	85.7
Msi2	5.6	83.8	96.4

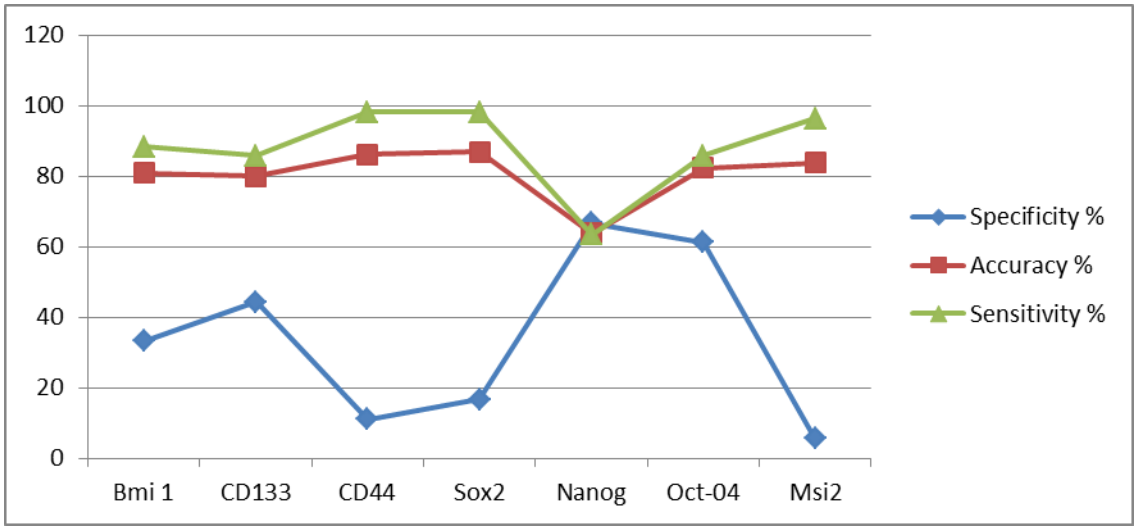

Fig. 1 Classifier's graphical analysis

Table 3 shows the specificity, accuracy and sensitivity values of stem cell associated markers mRNA in bronchoscopic biopsies. This has taken from lung cancer and non cancer patients. The highest sensitivity is CD44 (98.2%), Sox2 (98.2%) and Msi2 (96.4%). But their specificity were too low to be considered of no clinical significance. Nanog marker has the highest specificity 66.7% and the sensitivity is 63.4%. So, Bmi1,CD44 and CD133 are poor diagnostic markers for lung cancer. Nanog may serve as a promising diagnostic marker of lung cancer and potential therapeutic target in lung cancer.

3) Optimal procedure planning for peripheral bronchoscopy

Multidetector computed tomography scanners and Ultrathin bronchoscopes, the use of bronchoscopy for diagnosing peripheral lung cancer nodules is a option[7]. Image based planning and guidance system improves upon other systems.

TABLE IVV
Collection of Target ROI sites

SITE TYPE	**RUL**	**RML**	**RLL**	**LUL**	**LLL**	**TOTAL**
NODULE(< 3 cm)	4	5	3	9	1	22
MASS (>3 cm)	0	1	0	3	0	4
INFILTRATE	5	2	4	4	1	16
GGO	0	0	2	1	0	3
BAL site	3	1	0	0	0	4
Lymph Node	3	1	1	2	0	7
Other	3	2	2	3	3	13
Total	18	12	12	22	5	69

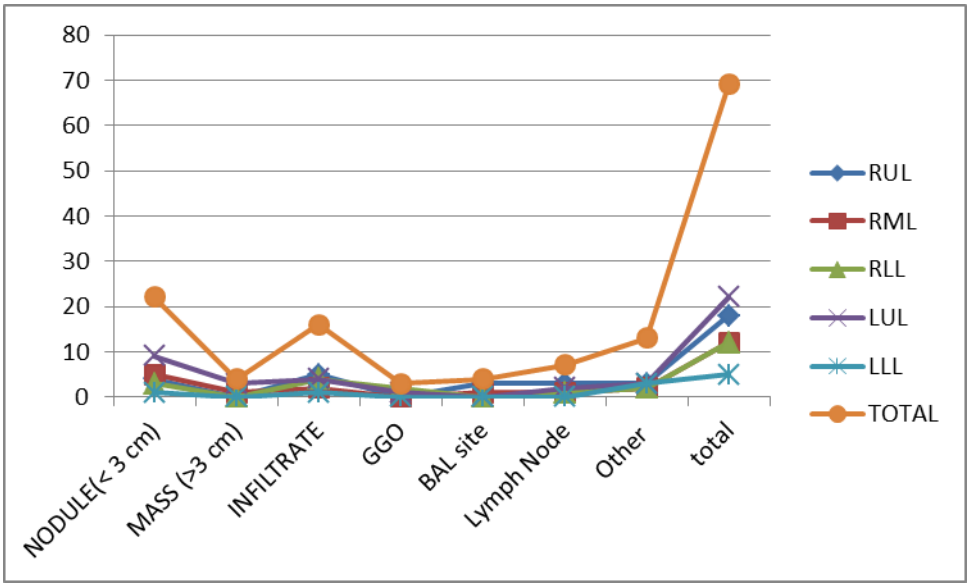

Fig. 2 Collection of Target RoI sites

Advances are,

- Optimal route planning which gives accurate airway routes to arbitrarily selected target sites.
- An interactive pre bronchoscopy report enables the physician to preview in advance.
- Integrates all views on one monitor during bronchoscopy
- Data fusion can be done during bronchoscopic navigation and ROI localization.
- Registration of the VB based guidance route with the bronchoscopic video.

As a comparison this ultrathin bronchoscopy study performed with insertion depth of 5.7 airways and a mean time to first sample of 8:30. Thus the automated system enabled bronchoscopy over 2 airways deeper into the airway tree periphery with a sample time that was 2 min shorter on average.

4) Algorithm for video summarization of bronchoscopy procedures

The time duration of bronchoscopy lesion findings varies considerably depending on the diagnostic and therapeutic procedures[14]. In videobronchoscopy, the whole process can be recorded as a video sequence. The bronchoscopist who initiates the recording process and usually chooses to archive only selected views and sequences. Video recordings registered during bronchoscopies include a considerable number of frames of poor quality due to blurry or unfocused images. It seems that such frames are unavoidable due to the relatively tight endobronchial space, rapid movements of the respiratory tract.

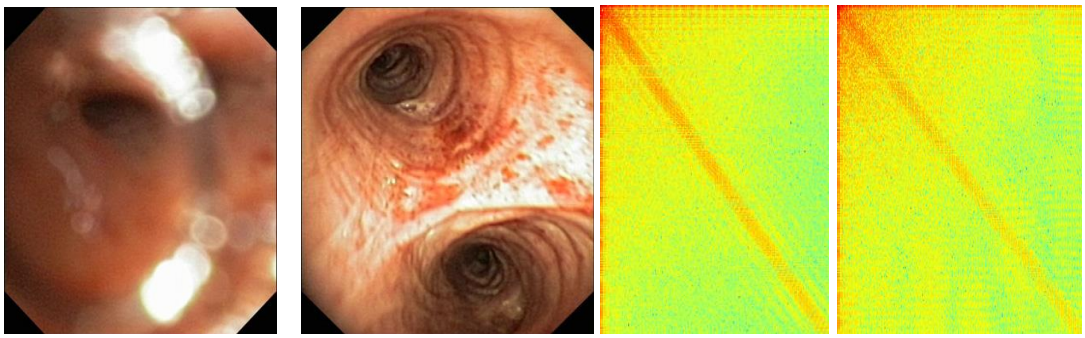

Fig 3(a): Example of 'non-informative' frame (b) Example of informative frame (c) Freequecy spectrum of 'non-informative' frame (d) Freequecy spectrum of 'informative' frame

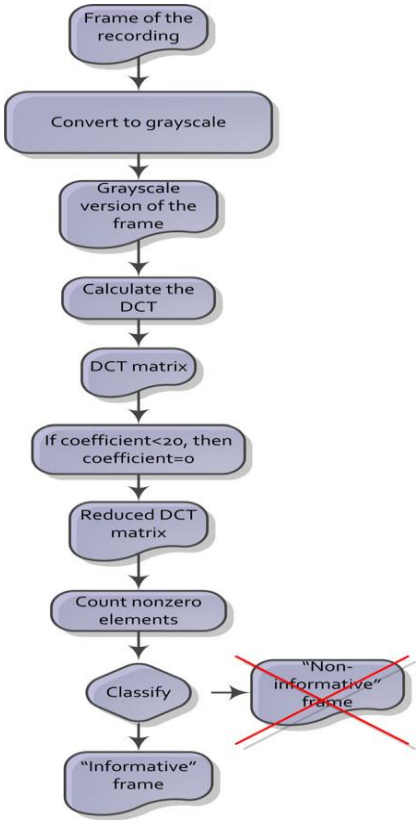

Fig 4: The classification algorithm based on the Discrete Cosine Transform for "informative" and "non-informative" frames.

5) Applications to biopsy path planning in virtual bronchoscopy in CT Images

The volumetric data of the human body can be measured precisely by 3D Medical imaging devices. The CAD systems give a lot of output images in a short interval of time. It is expected to reduce doctor's load and helping in accurate diagnosis. When a user inputs the target zone where there is suspicion of cancer, the CAD system displays a sequence of anatomical names of branches. The labelling accuracy was about 90%.

6) Automatic centerline extraction for 3D virtual bronchoscopy

We have an algorithm in this paper to the automatic determination of centreline of the bronchial branches. Centerline is the approximate centre of the bronchial tube which has maximum space for bronchoscopy to go about. First we determine the centreline of the three dimensional virtual bronchoscopy 3D image. Initially, a lot of end points in the binary tree which links up all centre points are constructed. Next, the endpoints of the lung airway tips are extracted. The centreline algorithm reads all the endpoints and suggests all the shortest paths from the start to those end points. Then , modified Digikstra[13] short path algorithm is applied to get the centreline of the bronchus.

7) ManiSMC – Manifold Modelling and Sequential Monte Corlo Sampler for boosting navigated bronchoscopy

We can track the bronchoscope's motion using ManiSMC and improve the navigation of Bronchoscopy. There are two stages in ManiSMC system. We extend local and global regressive Mapping method (LGRM)[16] to get bronchoscopic image sequences and construct their manifolds. With this, we can classify the specific scenes to specific branches. Next, we employ SMC sampler to integrate the data of stage, refine positions and orientations of bronchoscopy. Experimental results suggests that this method of navigation is highly effective. The advantage of this method is that we do not need an additional position sensor.

8) High definition bronchoscopy

Videobronchoscopy is an essential diagnostic procedure in bronchoscopic diagonisis of lung cancer[43]. High definition (HD) and advanced real time image enhancement techniques (i-scan) can be used to further enhance the navigation of bronchocopy[15].

III. CONCLUSIONS

In conclusion we have highlighted the bronchoscopic options for treatment of MAO which includes immediate and delayed effect modalities . Patient selection should exclude patients with short life expectancy limited symptoms and inability to visualize beyond the obstruction. The decision to treat should be made with other modalities such as external beam radiation in a multidisciplinary mode. In the optical procedure, comparing two videos of bronchoscopy and MDCT and finalising the lesion sample we treat cancer . The NPV classifier decides when bronchoscopy is non diagnostic.

In video branchoscopy calculating DCT matrix from grayscal frame and counting nonzero elements can classify the informative from noninformative frame.The centreline algorithm and modified Digikstra short path algorithm is used to get the centreline of the bronchus. The SMC sampler can be integrate the data of stage , refine orientation of bronchoscopy. Navigation of bronchoscopy can be enhanced by HD and iscan.

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