Reduction of under-reporting of occupational lung cancer (OLC) by lung tissue light mineralogic analysis (LTLMA) associated to standardized questionnaire (SQ). About fifty-nine cases

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I - INTRODUCTION

In France recognition of OLC is considered as insufficient. Moreover some asbestos or other inorganic dust exposure may be related to an environmental factor. Since 2002 SQ, introduced by a common action of the French Pneumology Society and the French Occupational Society, has reduced this underestimation. For operated lung cancer patients, LTLMA may also improve dust disease's recognition (1). Finally combination of SQ and LTLMA could offer to operated lung cancer patients the best approach to identify OLC and other environmental lung cancer (ELC).

II - POPULATION AND METHODS

A) Population (Table 1)

Population : 59 patients recruited between July 2004 and December 2008 among 510 new lung cancers underwent thoracic surgery with systematic LTLMA. Table 1 gives patients characteristics : 46 males, 13 females, 50 smokers or ex smokers, mean age : 64 years, 19 Stage I (42%), 12 Stage II (20%), 19 Stage III (32%), 3 Stage IV (6%). Pulmonary biopsy was systematically realized after resection (54 cases) or thoracotomy or thoracoscopy (5 cases) from lung tissue without tumour involvement.

Table 1

Description population n = 59			
Range age	38 – 84 years (mean 64)	Sexe	Female : 13 (22 %) Male : 46 (78 %)
Smoking history	Non smoker : 9 (15 %)	Smoker or ex smoker : 50 (85 %)	
Stage	Ia : 8 (13,5 %) Ib : 17 (28,8 %) IIa : 7 (11,8 %) IIb : 5 (8,5 %) IIIa : 10 (16,9 %) IIIb : 9 (15,3 %) IV : 3 (5,2 %)		
Surgical indication	Resection : 54 (91 %) Thoracotomy : 1 (1,7 %) Thoracoscopy : 4 (6 %)		
Cancer histology	Squamous cell (sq) 24 (40,6 %) Adenocarcinoma (adc) 29 (49,2 %) Bronchioloalveolar 2 (3,4 %) Small cell (sc) 1 (1,7 %) Large cell (lc) 2 (1,7%) Sarcoma 1 (1,7 %)		
Other pathologic lesion	Parietal pleural plaques 6 (10%) Granulomatosis 3 (5 %) Diffuse fibrosis 1 (1,7 %) Silicotic lymph node 2 (3,4 %)		

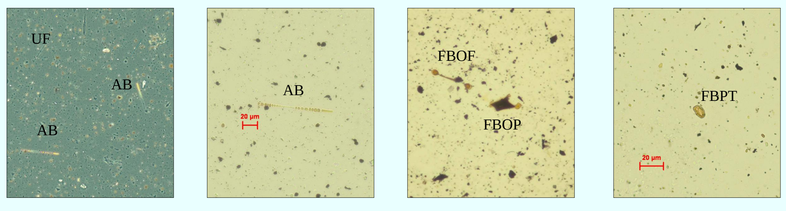
B) Occupational enquiry

SQ was submitted patient during lung cancer announcement consultation by medical team.
If SQ was not documented, principal occupational activities notified in patient's observation were analysed in correlation with SQ

C) Lung Tissue Light Mineralogic Analysis

Preparation samples : specimens were digested by sodium hypochlorite and collected on cellulose esters filters (pore size : 0,45 µm), dried and fixed on glass slides by fusion in acetone vapours.
Light microscopy : magnification x 400, transmitted light and phase contrast.
Counting : asbestos bodies (AB), uncoated fibres (UF) longer than 15 µm, ferruginous bodies (FB) on opaque fibre (FBOF), FB on opaque particle (FBOP) and FB on transparent particle (FBTP) with the largest diameter of particles greater than 15 µm (fig 1).
Results are expressed in g^{-1} of dry weight of lung tissue (gdw).
Dusty level estimation : A : low, B : intermediate, C : high

Figure 1



D) Statistical analysis

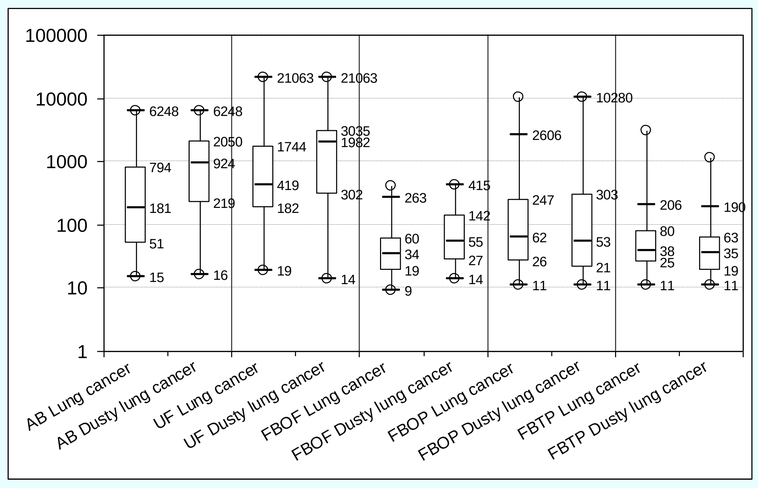
Descriptive statistics (geometric mean, median, quartiles 25%, 75%) are used to describe the features of the data in this study. The Wilcoxon matched-pairs signed-rank test was used for comparison of the particle concentrations observed between this lung cancer population and our control population pulmonary tissue. A p value below 0,05 was considered significant. All analyses were done using R (http://www.r-project.org).

III - RESULTS

A) Lung cancer cases : figure 2 describes the data of the 59 lung cancer series.
The geometric mean of AB, UF, FBOF, FBOP and FBTP are respectively : 190, 445, 44, 85 and 49 gdw.

B) Dusty lung cancers : table 2 reports sex, smoking habit, age, histology, clinical stage of the 20 OLC and 2 environmental non OLC selected combining SQ and LTLMA. Figure 2 describes the data of this 22 dusty lung cancer series. The geometric mean of AB, UF, FBOF, FBOP and FBTP are respectively : 586, 1140, 60, 214 and 79 gdw.

Figure 2



Patients	Sex	Smoking habit	Age	Histo logy	Stage	Occupation	AB	UF	FBOF	FBOP	FBTP	Dusty level	Other characteristics
TOU…	M	0	63	adc	IIIb	welder/pipefitter	250	2 415	42	42	42	A	Pleural plaques
GON…	M	12	73	adc	Ib	boiler/powerplant worker	1 440	1 989	34	940	206	C	Pleural plaques
SEB…	M	40	67	lc	Ia	construction worker	2 141	3 087	50	50	50	C	Pleural plaques
BOU…	M	50	75	sq	IIIb	oil/chemical refinery	916	204	34	69	34	B	Pleural plaques
MAT…	M	80	61	sq	IIIb	boiler/power plant worker	1 677	5 638	25	25	25	B	Pleural plaques
PON…	M	60	60	adc	IV	shipyard worker	3 115	12 078	263	263	131	C	Pleural plaques
BAR…	M	30	78	sq	Ib	boiler/powerplant worker	1 799	2 548	150	225	37	C	
MOU…	M	25	66	adc	IIIa	sheet metal worker	933	311	415	217	52	C	
PAU…	M	0	52	adc	Ib	insulator/pipe worker	810	4 284	26	104	104	C	
LEG…	M	30	59	sq	Ib	electrician	6 248	2 016	134	941	3 091	C	
IBN…	M	40	51	adc	Ib	shipyard worker	16	299	16	1 843	16	B	
VIA…	M	40	74	sc	IIb	oil/chemical refinery	3 660	8 320	104	247	35	C	
MAK…	M	40	53	adc	IIIa	insulator/pipe coverer	131	655	65	65	67	B	
REY…	M	45	66	bac	Ib	shipyard worker	2 167	21 063	165	329	27	C	
GIR…	M	50	72	sq	IIb	oil chemical refinery	17	87	14	14	14	A	
FOU…	M	60	60	sq	IIIa	foundry worker	298	1 376	145	362	36	C	
NAJ…	M	80	72	adc	Ia	brake repairman	1 401	267	200	467	1 134	C	
GRE…	M	90	59	sq	IIIb	sheet metal worker	5 649	2 885	60	481	60	C	
MED…	M	30	58	sq	IIIb	insulator and foundry worker	32	195	32	325	65	C	Interstitial fibrosis
BEN…	M	0	69	adc	IIIa	construction worker	210	745	23	186	740	B	Silicotic lymph node
OUR…	M	0	60	adc	IIIb	store-keeper	209	14	19	10 280	190	C	Silicotic lymph node
MAD…	F	0	54	adc	Ia	commercial	263	1 976	66	66	66	B	

C) Non smoker lung cancers

Table 3 reports the results of the 9 non smoker lung cancers. The geometric mean of AB, UF, FBOF, FBOP and FBTP are respectively : 145, 316, 36, 114 and 79 gdw.

Patients	Sex	Age	Histo logy	Stage	Occupation	AB	UF	FBOF	FBOP	FBTP	Dusty level	Other characteristics
PAU…	M	52	adc	Ib	insulator/pipe coverer	810	4 284	26	104	104	C	Asbestos OLC
OUR…	M	60	adc	IIIb	store keeper	209	14	19	10 280	190	C	Silicotic lymph node
MEL…	F	55	adc	IIIa	store keeper, chemical industry	35	419	35	35	35	B	Pleural plaques
TOU…	M	63	adc	IIIb	welder/pipe fitter	250	2 415	42	42	42	A	Pleural plaques, asbestos OLC
MAD…	F	54	adc	Ia	commercial	263	1 976	66	66	66	B	Granulomatosis, dusty nodes and dusty hobby
GRA…	F	72	sarcoma	Ia	store-keeper	19	39	19	19	19	C	Breast radiotherapy
BOV…	F	59	bac	Ib	housewife	171	43	43	43	43	A	
BEN…	M	69	adc	IIIa	construction worker	210	745	23	186	740	B	Silicotic lymph node
BIK…	F	43	sqc	Ia	cleaning woman	105	210	105	210	105	B	Granulomatosis

IV - DISCUSSION

1/ Improvement of OLC identification by combination SQ and LTLMA

A) LTLMA and lung cancer

- Mollo et al (2) among 924 non selected surgical cases of lung carcinoma report 116 cases (12,5%) with more than 1000 AB/gdw
- Dumortier et al (3) in a multi-centre retrospective study of 1931 cases, report 13,3 % cases with high level AB
- Our 10/59 (16%) patients with high level in this monocentric study are in accordance with other studies. Among 8 other asbestos occupational cases, 2 patients present elevation AB level at 900 and 930 near the threshold et 2 high level UF. Comparing the data of the 59 lung cancers with our population control (autopsy of subjects resident in an urban and peri-urban setting, not occupationally exposed to industrial dusts and with no pneumoconiosis), means of AB and UF are significantly different with a p-level < 0.05.

B) Standardized Questionnaire

In Legrand Cattan (4) mono-centric prospective study among 207 LC, only 122 (58%) could respond to a complete SQ. Among them 32 (26% of SQ completed and 15% LC population) could have claim for compensation.
SQ may be often incomplete in clinical practice : bad clinical status patient, linguistic barrier, refusal or forgetting patient, many temporary occupational activities, only surgical hospitalisation

C) Combination of SQ and LTLMA

This combination allows to identify 20 OLC, 18 asbestos OLC, 2 silica OLC. For 8/20 patients, LTLMA is essential before confirmation by SQ data. Moreover, 2 environmental dusty lung cancers are identified : one case with dusty construction hobby and one with silicotic lymph node and very high FBOP level.
So combination SQ and LTLMA may identify 37% dusty lung cancer and may improve claim for compensation.

2/ LTLMA and non smoker lung cancer

9 (5 females, 4 males)/59 patients (15%) are non smoker lung cancer. This level is in accordance with Wakelee Study (5). Several etiologic factors have been proposed : domestic radon, indoor pollutants, previous lung disease and genetic factors play a role, but LTLMA may help active enquiry .
We identify among nine patients, 3 OLC and 2 environmental non OLC, 1 breast radiotherapy induced LC, 1 sarcoidosis case, and two cases without identified specific aetiology or association. Electron microscopy and microanalysis studies are under investigation.

V - CONCLUSION

The addition of LTLMA to SQ improves occupational or environmental non occupational lung cancer recognition. Systematic LTLMA or specimen stocking are recommended specially after lung cancer resection and for low or non smoker. Mineralogic analysis may be realised only if SQ is insufficient .

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