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CT characteristics of resolving ground-glass opacities in a lung cancer screening programme

L. Felix[a], G. Serra-Tosio[a], S. Lantuejoul[b,c], J.F. Timsit[c], D. Moro-Sibilot[c,d], C. Brambilla[c,d], G.R. Ferretti[a,c,*]

[a] Clinique Universitaire de Radiologie et Imagerie Médicale, Université Grenoble I, CHU Grenoble, France
[b] Département d'anatomie Pathologique, Université Grenoble I, CHU Grenoble, France
[c] INSERM U823, A Bonniot Institute, La Tronche, France
[d] Clinique Universitaire Pneumologique, Université Grenoble I, CHU Grenoble, France

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ABSTRACT

Purpose: This study aimed at evaluating the computed tomography (CT) characteristics of resolving localized ground-glass opacities (GGOs) in a screening programme for lung cancer.
Material and methods: 280 patients at high-risk for lung cancer (221 men, 59 women; mean age, 58.6 years), divided into four groups (lung cancer history ($n = 83$), head and neck cancer history ($n = 63$), symptomatic ($n = 88$) and asymptomatic ($n = 46$) cigarette smokers), were included in a prospective trial with annual low-dose CT for lung cancer screening. We retrospectively reviewed all localized GGOs, analyzed the CT characteristics on initial CT scans and changes during follow-up (median 29.1 months). Variables associated with resolution of GGOs were tested using chi-square or Mann–Whitney tests.
Results: A total of 75 GGOs were detected in 37 patients; 54.7% were present at baseline and 45.3% appeared on annual CT. During follow-up, 56.2% persisted and 43.8% disappeared. The resolving localized GGOs were significantly more often lobular GGOs ($p = 0.006$), polygonal in shape ($p = 0.02$), mixed ($p = 0.003$) and larger ($p < 0.0001$) than non-resolving localized GGOs.
Conclusion: Localized GGOs are frequent and many disappeared on follow-up. CT characteristics of resolving GGOs show significant differences compared to persistent ones. This study emphasizes the importance of short-term CT follow-up in subjects with localized GGOs.

1. Introduction

The widespread use of computed tomography (CT) in clinical practice and for lung cancer screening had lead to increase the detection of localized ground-glass opacities (GGOs) in the peripheral lung [1]. On high-resolution CT scans, ground-glass opacity (GGO) appears as hazy increased attenuation of lung, with preservation of bronchial and vascular margins [2]. It is caused by partial filling of airspaces, interstitial thickening (due to fluid, cells, and/or fibrosis), partial collapse of alveoli, normal expiration, increased capillary blood volume, or a combination of these, the common factor being the partial displacement of air [2]. It is known that GGO is a non-specific finding, and the appearance of a focal area of GGO on thin-section CT images can indicate a variety of benign or malignant disorders. Malignant aetiologies include bronchioloalveolar carcinoma, early-stage adenocarcinoma and sometimes metastases [3–11]. Benign aetiologies include infectious and inflammatory diseases, focal haemorrhage, focal interstitial fibrosis, and precancerous lesion such as atypical alveolar hyperplasia [8–14]. Several studies have found that the frequency of malignancy in localized GGOs was higher than in solid nodules [7,9,15–17].

Localized GGOs have been classified as mixed localized GGOs or pure localized GGOs according to the presence or the absence of a solid component with soft tissue density completely obscuring the lung parenchyma and the contour of the vessels with which it is in contact.

This study was designed in order to analyze localized GGOs in a CT screening for lung cancer in a European population so as to establish the natural history of localized GGO and to identify predictive factors for resolving lesions. Correlating the CT characteristics of GGOs to histological findings was out of scope of this study.

2. Material and methods

2.1. Participants

The institutional review board's approval and the participants' written informed consent were obtained. This study was based on a

* Corresponding author at: Service Central de Radiologie et Imagerie Médicale, INSERM U823, CHU Grenoble BP 217, F-38043 Grenoble cedex 09, France.
Tel.: +33 476 769 290; fax: +33 476 765 901.
E-mail address: gferretti@chu-grenoble.fr (G.R. Ferretti).

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local screening program for lung cancer in high-risk patients using annual helical high-resolution low-dose CT from October 2001 to June 2007. A total of 280 individuals were included in this prospective trial. The participants were distributed into four groups: group 1, patients with history of lung cancer (operated and in remission) ($n = 83$; 29.6%); group 2, patients with history of head and neck cancer (treated and in remission) ($n = 63$; 22.5%); group 3, current or former cigarette smokers with respiratory symptoms (cough or dyspnoea) ($n = 88$; 31.4%); and group 4, asymptomatic patients with a history of cigarette smoking of at least 15 cigarettes per day during at least 20 years, current or former (i.e., they quit less than 15 years ago) ($n = 46$; 16.4%). Current smokers included in the study were incited to enter our local smoking cessation programme.

At inclusion, participants were considered to be without a serious illness that would decrease life expectancy and they were considered fit to undergo thoracic surgery (patients without congestive heart failure or disabling dyspnoea). Ineligible were those who could not be followed annually, current pregnancy, or patients with anticoagulant treatment or a disease with hemorrhagic propensity, as well as those with a history of any cancer within the past 5 years other than non-melanomatous skin cancer, resected lung cancer, or head and neck cancer in remission.

There were 221 (79%) men and 59 women (21%), 274 smokers (98%) (Pack years range, 6–90; mean, 40) and 6 non-smokers but with history of lung cancer (2%). The mean age of the subjects at the initial CT screening was 58.6 years (age range, 33.9–80 years).

2.2. CT imaging

All CT scans were acquired at the end of inspiration, with a 16-detector row CT scanner (Sensation 16, Siemens medical Solutions, Erlangen, Germany) using the following parameters: 0.75-mm slice collimation, exposure time of 0.5 s, table feed of 18 mm per rotation, 120 kVp, and 60–80 mAs. The data were reconstructed into 1-mm-thick sections with 0.8-mm intervals using a high-resolution reconstruction kernel and displayed at standard window setting (width, 1600 HU; level, −400 HU). No intravenous contrast materiel was administered with exception of patients with history of lung cancer in whom a complementary examination of the liver and adrenal glands was performed.

2.3. Image reading and data analysis

All CT scans were prospectively read at a computer workstation by an experienced thoracic radiologist who recorded all the detected nodules. Images were viewed using both cine-mode and maximum intensity projections in the trans axial plane [18].

In the first part of the study, we considered all pulmonary non-calcified nodules detected at baseline screening. Each nodule was classified according to its density as solid nodule, pure nodular GGO or mixed nodular GGO. We then determined the frequency of occurrence of the different types of non-calcified nodules.

In the second part, two radiologists (an experienced thoracic radiologist and a junior radiologist (5th year resident)) retrospectively reviewed in consensus all the CT scans of patients with localized GGOs < 3 cm in diameter.

The images were then viewed at a computer workstation, in axial, frontal, and sagittal planes. The CT characteristics of each lesion were analyzed as follows: type (nodular, lobular or flat ground-glass opacity), size (axial diameter and height), shape in the axial plane (round, oval, complex, or polygonal), shape in the other planes (round, oval, complex, polygonal, or flat), margins (smooth, somewhat irregular, or spiculated/concave or convex), and density (pure localized GGO or mixed localized GGO).

On follow-up CT or annual CT scans, we recorded changes in number of localized ground-glass opacities (appearance, stability, or disappearance) and assessed any changes in persistent lesions, e.g., size, shape, marginal characteristics, and density.

We finally compared CT characteristics of resolving localized GGOs to those of non-resolving localized GGOs.

Localized GGOs were categorized in nodular GGOs with round, oval or complex shapes in the three planes, lobular GGOs with polygonal shapes in the three planes, and flat GGOs with round, oval, complex or polygonal shapes in the axial plane but with a flat shape in the frontal and sagittal planes.

The axial diameter of a nodule was defined as the average length and width measured on the image showing the largest cross-sectional area. Subsequently, we categorized solid nodules and

Table 1
Size (axial diameter) and type distribution of nodules at baseline screening.

	<5 mm	5–10 mm	10–20 mm	20–30 mm	Total (%)
Solid	213	92	17	3	325 (89.8)
NGGO	5	26	5	1	37 (10.2)
pNGGO	5	22	3	0	30 (8.3)
mNGGO	0	4	2	1	7 (1.9)
Total (%)	218 (60.2)	118 (32.6)	22 (6.1)	4 (1.1)	362 (100)

NGGO = nodular GGO, pNGGO = pure nodular GGO, mNGGO = mixed nodular GGO.

Table 2
Clinical characteristics of 37 patients with ground-glass opacities.

Sex	Male	26 (70%)
	Female	11 (30%)
Age (years)	Range: 37.1–80; mean: 59.1	
Group	History of lung cancer (1)	11 (30%)
	History of head and neck cancer (2)	9 (24%)
	Symptomatic smokers (3)	8 (22%)
	Asymptomatic smokers (4)	9 (24%)
Smoking history	Current and former smokers	37 (100%)
	Current smokers	12 (32,4%)
	Former smokers	25 (67.6%)
	Pack years	Range: 15–72; mean: 38

Table 3
CT characteristics of 75 ground-glass opacities in 37 patients.

Type	Nodular GGO	63 (84%)
	Lobular GGO	6 (8%)
	Flat GGO	6 (8%)
Size	Axial diameter (mm)	Range: 2.5–27.4; mean: 8.4
	Height (mm)	Range: 1.7–29.8; mean: 6.9
Shape in the axial plane	Round	43 (57.3%) (1 flat GGO)
	Oval	5 (6.7%)
	Complex	19 (25.3%) (3 flat GGOs)
	Polygonal	8 (10.7%) (2 flat GGOs)
Shape in the others planes	Round	42 (56%)
	Oval	5 (6.7%)
	Complex	16 (21.3%)
	Polygonal	6 (8%) (=6 lobular GGOs)
	Flat	6 (8%) (=6 flat GGOs)
Margins type 1	Smooth	43 (57.3%)
	Slightly irregular	27 (36%)
	Spiculated	5 (6.7%)
Margins type 2	Convex	61 (31.3%)
	Concave	14 (18.7%)
Density		
Pure GGO	59 (78.7%)	
	Internal attenuation (UH): range: −864 to −169; mean: −582	
Mixed GGO	16 (21.3%)	
	GGO < 50%	11 (69%)
	GGO ≥ 50%	5 (31%)

Table 4
Size (axial diameter) and type distribution of localized GGOs.

	<5 mm	5–10 mm	10–20 mm	20–30 mm	Total (%)
Nodular GGOs	14	32	9	8	63 (84)
Lobular GGOs	0	0	5	1	6 (8)
Flat GGOs	0	2	4	0	6 (8)
Total (%)	14 (18.7)	34 (45.3)	18 (24)	9 (12)	75 (100)

ground-glass opacities' size into four groups: <5 mm, ≥5 mm and <10 mm, ≥10 mm and <20 mm, and ≥20 mm and <30 mm.

The height of localized GGOs was also recorded in the frontal or sagittal reformations so as to distinguish flat opacities from nodular and lobular opacities. The opacity was considered a "flat opacity" when the ratio between the axial diameter and the height was equal or superior to 2.

The term "oval shape" was used when the length was equal or more than 1.5 times width. The term "polygonal shape" was used to describe a lesion with linear or concave margins at every corner, and the term "complex shape" was used to describe all shapes other than those described as round, oval or polygonal.

In the case of mixed GGO, the radiologists assessed the percentage of GGO areas in the entire lesion [19]. A predominantly solid lesion was defined as a lesion of GGO < 50%, whereas a predominantly GGO lesion was defined as a lesion of GGO ≥50% [20].

Changes in size were recorded if there was a variation equal or superior to 20% between the lesion size on diagnostic CT scan and the lesion size in the last follow-up or annual CT scan.

2.4. Recommendations for the management of nodules

In this CT screening for lung cancer, nodules management recommendations were based on the size and density of nodules. For solid nodules and mixed nodular GGOs < 5 mm and for pure nodular GGOs < 10 mm, only annual repeat screening was performed.

For solid nodules and mixed nodular GGOs ≥ 5 mm and for pure nodular GGOs ≥ 10 mm, complementary investigations (follow-up CT scans performed at 1 and 3 months after antibiotic treatment or nodule biopsy (bronchoscopically-guided biopsy, percutaneous transthoracic biopsy, or surgical biopsy)) were necessary and discussed for each case in a multidisciplinary clinic including a pulmonary oncologist, a radiologist and a thoracic surgeon.

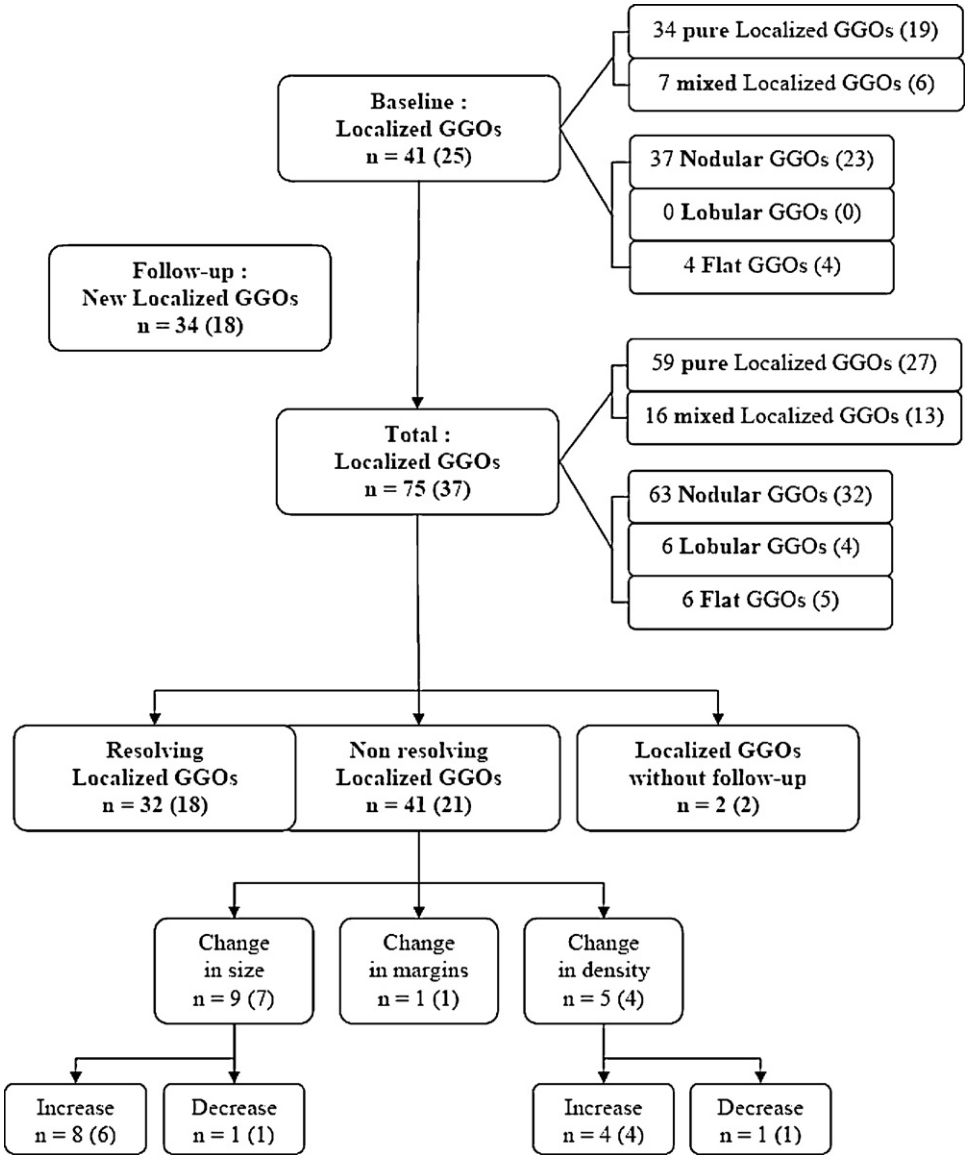

Fig. 1. Natural history of localized GGOs (number of patients).

2.5. Statistical analysis

The characteristics of the patients and of the GGOs are presented as mean ± SD and *n* (%) where appropriate. Variables associated with the resolution of GGOs were tested univariately using chi-square or Mann–Whitney tests whilst taking into consideration the independence of the resolution of nodules within patients SAS (SAS institute) 9.13 statistical software was used.

3. Results

3.1. Frequency and description of the different types of nodules at baseline screening

Three hundred sixty-two nodules were found on 280 CT scans analysed at baseline screening. The size (axial diameter) and density distribution of non-calcified nodules are given in Table 1.

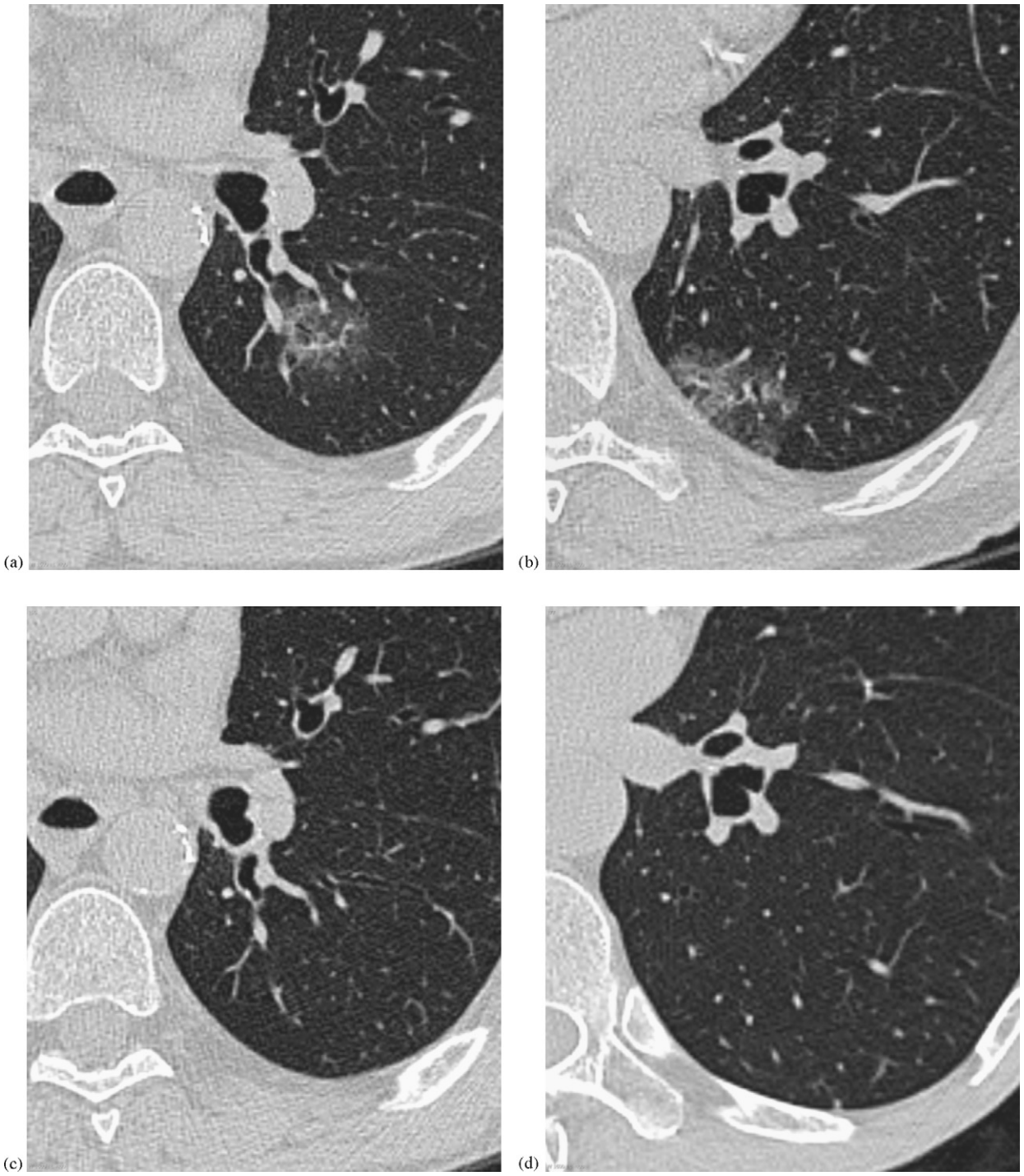

Fig. 2. A 67-year-old man with a history of cigarette smoking and head and neck cancer. (a and b) Transverse high-resolution CT scan shows two localized ground-glass opacities in the left lower lobe: a 23-mm round pure ground-glass opacity (a) and a 26.5-mm polygonal pure ground-glass opacity (b). (c and d) The two lesions are completely resolved on the follow-up CT scan 2 months later.

3.2. Natural history of localized GGOs (Fig. 1)

From October 2001 to June 2007, a total of 867 CT scans were performed on 280 patients. One or more localized ground-glass opacities were found in 37 (13.2%) of the 280 individuals. These 37 patients have had a total of 172 CT scans (mean: 4.6 per patient; range 3–8) and were followed from 11.5 to 51 months (median follow-up, 29.1 months (875 days)). Demographic and clinical characteristics of the 37 patients are presented in Table 2.

3.2.1. Prevalence of localized ground-glass opacities at baseline screening

At baseline screening, 41 localized GGOs were identified in 25 (8.9%) of the 280 participants, 7 were mixed GGOs (17%) and 34 were pure GGOs (83%). Eighteen individuals had a single lesion, five had two lesions, one had six lesions, and one had seven lesions.

3.2.2. Frequency of localized ground-glass opacities at baseline and annual repeat screenings

From October 2001 to June 2007, 75 localized GGOs were identified in 37 of the 280 participants. Twenty-one individuals had a single lesion, 11 had two lesions, 1 had three lesions, 1 had six lesions, 1 had seven lesions, and 2 had eight lesions. The CT characteristics of the 75 localized GGOS were presented in Table 3. The size (axial diameter) and type distribution of localized GGOs were given in Table 4.

3.2.3. Retrospectively diagnosed GGOs

Among 75 localized GGOs, 19 (25.3%) were retrospectively diagnosed in 13 patients. The delay varied between 2 and 50 months (mean, 23.5 months).

3.2.4. Changes on follow-up

3.2.4.1. Changes in number of GGOs. Out of 75 localized GGOs, 41 (54.7%) were present at baseline screening (prevalence, 14.6% (41/280)) and 34 (45.3%) appeared on annual repeat screenings in 1.5–15 months (mean, 10.7 months). On follow-up CT scans, 32 localized GGOs (42.7%) disappeared in 1.5–19 months (mean, 7.6 months), 41 localized GGOs (54.7%) were persistent and were followed from 9.5 to 50 months (mean, 26 months) and 2 newly localized GGOs (2.7%) (1 nodular and 1 flat) in two patients with previous localized GGOs have not yet been followed.

3.2.4.2. Changes in CT characteristics for persistent GGOs. On follow-up CT scans, none of the lesions showed any change in shape. Only one of the lesions showed change in marginal characteristics from concave to convex margins. Thirty-two localized GGOs (78.1%) were stable in size and were followed from 9.5 to 50 months (mean, 26 months), only one localized GGO (2.4%) decreased in size but increased in density, and eight localized GGOs (19.5%) increased in size, from 32% to 72% (mean, 52.5%), in a period of 18–50 months (mean, 30.8 months).

3.3. Resolving localized GGOs

During follow-up, 32 localized GGOs disappeared. We found that there were statistical differences between resolving and non-resolving localized GGOs for the following CT characteristics: type of localized GGOs, shape, size, and density (Table 5). Otherwise, the newly appeared localized GGOs were more often resolving than those that were present at baseline screening. Examples of resolving localized GGOs were presented in Figs. 2 and 3.

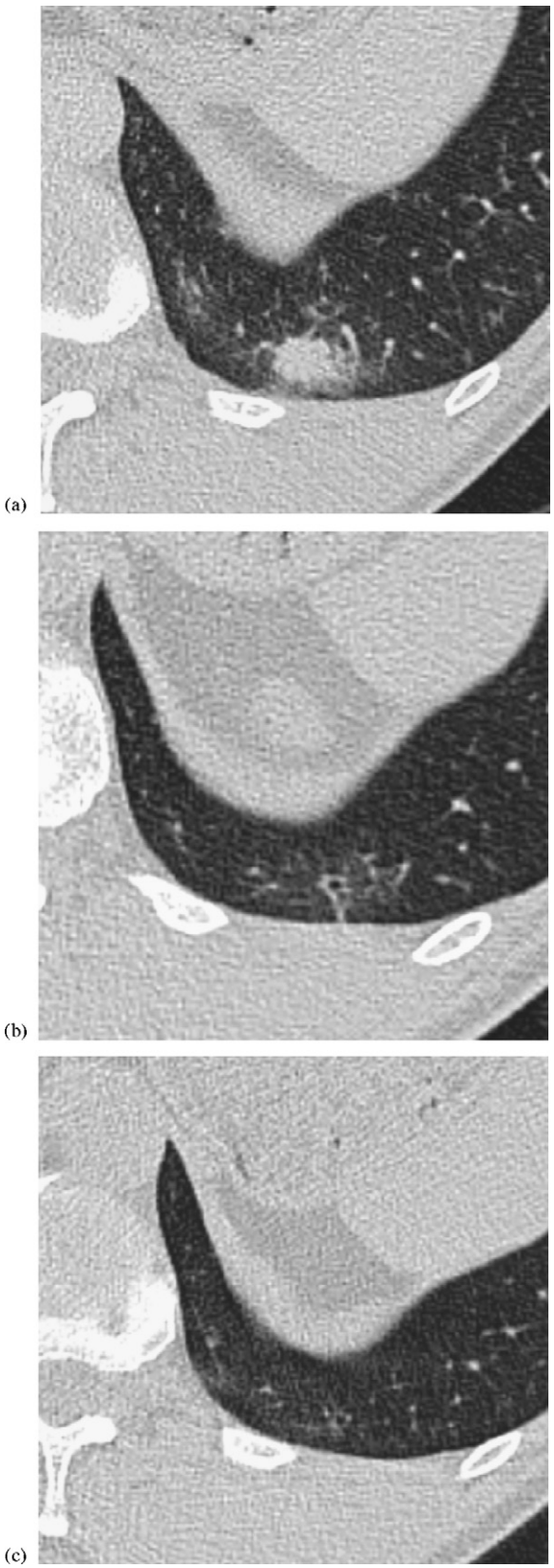

Fig. 3. A 52-year-old man with a history of cigarette smoking and a history of head and neck cancer. (a) Transverse high-resolution CT scan shows a 22-mm oval mixed ground-glass opacity in the left lower lobe, with a predominant solid pattern, slightly irregular and convex margins. (b) Two months later: the density changes from mixed to pure ground-glass opacity. (c) Seventeen months later: the lesion is completely resolved.

Table 5
CT characteristics of resolving and non-resolving localized ground-glass opacities for 73 followed GGOs in 35 patients.

Characteristics			Disappearance	No disappearance	*p*-value
Type	Nodular GGO ($n=62$)	Yes	25	37	0.2
		No	7	4	
	Lobular GGO ($n=6$)	Yes	6	0	0.006
		No	26	41	
	Flat GGO ($n=5$)	Yes	1	4	0.38
		No	31	37	
Size	Axial diameter (mm)		13.8 ± 7.3	7.4 ± 3.4	<0.0001
	Height (mm)		12.2 ± 7.9	5.9 ± 2.9	0.0002
Shape in the axial plane	Round		13	29	0.02
	Oval		3	2	
	Complex		9	9	
	Polygonal		7	1	
Shape in the other planes	Round		13	28	0.01
	Oval		3	2	
	Complex		9	7	
	Polygonal		6	0	
	Flat		1	4	
Polygonal shape in the axial plane		Yes	7	1	0.02
		No	25	40	
Density	Pure GGO		20	38	0.003
	Mixed GGO		12	3	
Newly appeared localized GGOs		Yes	23	9	<0.0001
		No	9	32	

3.4. Histological results for persistent GGOs

Five persistent localised GGOs were histologically confirmed in four patients. One subject underwent lateral thoracotomy with resection of a 14-mm mixed nodular GGO that was diagnosed as mixed adenocarcinoma with bronchioloalveolar component (stage IA). One subject underwent lateral thoracotomy with segmentectomy of a 11-mm pure nodular GGO that was diagnosed as a mixed adenocarcinoma with bronchioloalveolar component (stage IA); in the same procedure a pure flat GGO 10-mm in diameter, 4-mm height, was resected and diagnosed as localized desquamative interstitial pneumonia. In two individuals, one pure nodular GGO was resected, respectively, 15-mm and 10-mm in diameter; pathological analysis showed two atypical alveolar hyperplasia. Other cases are currently followed.

4. Discussion

4.1. Prevalence of nodular GGOs in comparison to solid nodules at baseline

At baseline screening, we found that nodular GGOs represent 10.2% of the 362 detected non-calcified pulmonary nodules. The prevalence of nodular GGOs is different according to studies as they represented 19% of the 233 positive results in the ELCAP (Early Lung Cancer Action Project) [7], 6.3% of the 4037 non-calcified pulmonary nodules in a lung cancer screening in Korea [15], and 7.7% of the 168 non-calcified nodules in a lung cancer screening in Ireland [21,22]. The differences in collimation (1-, 5- or 10-mm) and in reading methods (films versus workstation viewing) may explain these variations. Among nodular GGOs, pure nodular GGOs were more frequently described than mixed nodular GGOs (30 versus 7), which is consistent with the results of the ELCAP study (28 versus 16) [7].

4.2. Retrospectively diagnosed GGOs

According to a study conducted by Li et al. [23], 69% of lung cancers missed by radiologists at screening CT were nodules with GGO. Therefore, lesions with GGO were considered to be subtle or very subtle owing to poor conspicuity. This low conspicuity may lead to detection errors. In our study, this fact is illustrated by the percentage of lesions that were diagnosed retrospectively (25.3%).

4.3. Resolving localized GGOs

In our study, 32 (42.7%) of the 75 detected localized GGOs disappeared. These rates were respectively 13% (7/54) in the study of Vazquez and Flieder [24] and 45% (83/186) in the study of Oh et al. [25].

One of the aims of our study was to retrospectively analyze localized GGOs that resolved during follow-up and assess their CT characteristics in order to identify morphological features that could be helpful in an initial GGO classification (benign resolving opacities or non-resolving and therefore possibly malignant opacities). Diederich et al. [26] have already examined the CT characteristics of resolving nodules, but all types of nodules (solid, pure and mixed nodular GGOs) were included. They observed that resolving pulmonary nodules are mostly $\leq$10 mm, peripherally located, solid, well-defined, non-lobulated and most resolve completely within a variable interval, ranging from several days to years. However, they could not identify the morphological features that allow the differentiation between nodules that will or will not resolve during follow-up. Inversely, in our study we identified several CT characteristics that were significantly different between resolving and non-resolving localized GGOs.

The resolving localized GGOs were more frequently lobular GGOs ($p=0.006$) and more frequently have a polygonal shape in the axial and other planes ($p=0.02$ and $p=0.01$, respectively). Several investigators have suggested that a persistent nodule with a polygonal shape was in favour of benignity. According to Takashima et al. [3], a polygonal or flat shape may represent advanced scar tissue as result of an inflammatory process from a variety of causes and then the possibility of malignancy may be substantially low. In the present study, the resolving localized GGOs were more frequently mixed localized GGOs than pure localized GGOs ($p=0.003$). So the probabilities of disappearance were 34% (20/59) for pure localized GGOs and 75% (12/16) for mixed localized GGOs and most of dis-

appearances (16 of 20 pure localized GGOs and 11 of 12 mixed localized GGOs) were found on the first follow-up CT scan with a delay of 1.5 and 19 months (mean, 7.6 months). This delay was probably over-estimated as some localized GGOs were not followed within a short period of time. Oh et al. [25] have studied the natural history of solitary ground-glass opacities in 186 patients (69 pure GGOs and 117 mixed GGOs). They found that the probabilities of disappearance or regression were 37.6% (26/69) for pure GGOs and 48.7% (57/117) for mixed GGOs and that most of regressions and disappearances (23 of 26 non-solid GGOs and 56 of 57 part-solid GGOs) were found on the first follow-up CT scan, within 3 months.

In our series, the axial diameter and height were significantly higher for resolving localized GGOs than for non-resolving localized GGOs ($p = <0.0001$ and $p = 0.002$, respectively). Generally these characteristics of density and size were in favour of malignancy for persistent lesions [5,7,25]. These results confirm the interest of short-term CT follow-up for localized GGOs in order to differentiate benign resolving lesions and non-resolving and therefore possibly malignant lesions. However, as demonstrated by Kim et al. [27], non-resolving GGOs also include benign diseases, and no CT characteristics allow distinguishing benign from malignant lesions. The management of the persistent localized GGOs is then difficult and actually only surgical and histological examinations allow a sure diagnosis. Management of such pulmonary nodules may benefit from software analysis that allows reproducible and promising quantitative method for determining the grades of malignancy of small lung cancers [28]. Then, further studies will be necessary to improve the management of persistent localised GGOs.

4.4. Limits of study

Our histological results of persistent localised GGOs were limited as compare to studies from Asia, as GGOs are less frequent in European population than in Asian population.

5. Conclusion

Localized GGOs are a frequent finding on high-resolution CT scans in this high-risk population. They correspond to nodular, lobular, or flat opacities. Many of them disappeared on follow-up. Resolving GGOs are mostly lobular opacities, polygonal in shape, mixed GGOs, and greater in size than non-resolving GGOs. However, some CT characteristics are similar in resolving GGOs and malignant lesions, thus underlying the interest of short-term CT follow-up.

References

[1] Henschke CI, McCauley DI, Yankelevitz DF, et al. Early Lung Cancer Action Project: overall design and findings from baseline screening. Lancet 1999;354(9173):99–105.
[2] Hansell DM, Bankier AA, MacMahon H, McLoud TC, Muller NL, Remy J. Fleischner Society: glossary of terms for thoracic imaging. Radiology 2008;246(3):697–722.
[3] Takashima S, Sone S, Li F, et al. Small solitary pulmonary nodules (≤1 cm) detected at population-based CT screening for lung cancer: reliable high-resolution CT features of benign lesions. AJR Am J Roentgenol 2003;180(4):955–64.
[4] Li F, Sone S, Abe H, Macmahon H, Doi K. Malignant versus benign nodules at CT screening for lung cancer: comparison of thin-section CT findings. Radiology 2004;233(3):793–8.
[5] Nakata M, Saeki H, Takata I, et al. Focal ground-glass opacity detected by low-dose helical CT. Chest 2002;121(5):1464–7.
[6] Jang HJ, Lee KS, Kwon OJ, Rhee CH, Shim YM, Han J. Bronchioloalveolar carcinoma: focal area of ground-glass attenuation at thin-section CT as an early sign. Radiology 1996;199(2):485–8.
[7] Henschke CI, Yankelevitz DF, Mirtcheva R, McGuinness G, McCauley D, Miettinen OS. CT screening for lung cancer: frequency and significance of part-solid and nonsolid nodules. AJR Am J Roentgenol 2002;178(5):1053–7.
[8] Lee HJ, Goo JM, Lee CH, Yoo CG, Kim YT, Im JG. Nodular ground-glass opacities on thin-section CT: size change during follow-up and pathological results. Korean J Radiol 2007;8(1):22–31.
[9] Nakajima R, Yokose T, Kakinuma R, Nagai K, Nishiwaki Y, Ochiai A. Localized pure ground-glass opacity on high-resolution CT: histologic characteristics. J Comput Assist Tomogr 2002;26(3):323–9.
[10] Noguchi M, Morikawa A, Kawasaki M, et al. Small adenocarcinoma of the lung. Histologic characteristics and prognosis. Cancer 1995;75(12):2844–52.
[11] Park CM, Goo JM, Lee HJ, Lee CH, Chun EJ, Im JG. Nodular ground-glass opacity at thin-section CT: histologic correlation and evaluation of change at follow-up. Radiographics 2007;27(2):391–408.
[12] Collins J, Stern EJ. Ground-glass opacity at CT: the ABCs. AJR Am J Roentgenol 1997;169(2):355–67.
[13] Park CM, Goo JM, Lee HJ, et al. CT findings of atypical adenomatous hyperplasia in the lung. Korean J Radiol 2006;7(2):80–6.
[14] Park CM, Goo JM, Lee HJ, et al. Focal interstitial fibrosis manifesting as nodular ground-glass opacity: thin-section CT findings. Eur Radiol 2007;17(9):2325–31.
[15] Chong S, Lee KS, Chung MJ, et al. Lung cancer screening with low-dose helical CT in Korea: experiences at the Samsung Medical Center. J Korean Med Sci 2005;20(3):402–8.
[16] Yoon HE, Fukuhara K, Michiura T, et al. Pulmonary nodules 10 mm or less in diameter with ground-glass opacity component detected by high-resolution computed tomography have a high possibility of malignancy. Jpn J Thorac Cardiovasc Surg 2005;53(1):22–8.
[17] Yang ZG, Sone S, Takashima S, et al. High-resolution CT analysis of small peripheral lung adenocarcinomas revealed on screening helical CT. AJR Am J Roentgenol 2001;176(6):1399–407.
[18] Jankowski A, Martinelli T, Timsit JF, et al. Pulmonary nodule detection on MDCT images: evaluation of diagnostic performance using thin axial images, maximum intensity projections, and computer-assisted detection. Eur Radiol 2007;17(12):3148–56.
[19] Takashima S, Li F, Maruyama Y, et al. Discrimination of subtypes of small adenocarcinoma in the lung with thin-section CT. Lung Cancer 2002;36(2):175–82.
[20] Takashima S, Sone S, Li F, Maruyama Y, Hasegawa M, Kadoya M. Indeterminate solitary pulmonary nodules revealed at population-based CT screening of the lung: using first follow-up diagnostic CT to differentiate benign and malignant lesions. AJR Am J Roentgenol 2003;180(5):1255–63.
[21] MacRedmond R, Logan PM, Lee M, Kenny D, Foley C, Costello RW. Screening for lung cancer using low dose CT scanning. Thorax 2004;59(3):237–41.
[22] MacRedmond R, McVey G, Lee M, et al. Screening for lung cancer using low dose CT scanning: results of 2 year follow up. Thorax 2006;61(1):54–6.
[23] Li F, Sone S, Abe H, MacMahon H, Armato 3rd SG, Doi K. Lung cancers missed at low-dose helical CT screening in a general population: comparison of clinical, histopathologic, and imaging findings. Radiology 2002;225(3):673–83.
[24] Vazquez MF, Flieder DB. Small peripheral glandular lesions detected by screening CT for lung cancer. A diagnostic dilemma for the pathologist. Radiol Clin North Am 2000;38(3):579–89.
[25] Oh JY, Kwon SY, Yoon HI, et al. Clinical significance of a solitary ground-glass opacity (GGO) lesion of the lung detected by chest CT. Lung Cancer 2007;55(1):67–73.
[26] Diederich S, Hansen J, Wormanns D. Resolving small pulmonary nodules: CT features. Eur Radiol 2005;15(10):2064–9.
[27] Kim HY, Shim YM, Lee KS, Han J, Yi CA, Kim YK. Persistent pulmonary nodular ground-glass opacity at thin-section CT: histopathologic comparisons. Radiology 2007;245(1):267–75.
[28] Sumikawa H, Johkoh T, Nagareda T, et al. Pulmonary adenocarcinomas with ground-glass attenuation on thin-section CT: quantification by three-dimensional image analyzing method. Eur J Radiol 2008;65(1):104–11.