Chest CT evaluation of 11 persistent asymptomatic patients with SARS-CoV-2 infection

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Running head: CT of asymptomatic patients with SARS-CoV-2

Summary

Eleven asymptomatic carriers who received nasal or throat swab test for SARS-CoV-2 after close contacts with patients who developed symptomatic 2019 coronavirus disease (COVID-19) were enrolled in this study. The chest CT images of enrolled patients were analyzed qualitatively and quantitatively. There were 3 (27.3%) patients had normal first chest CT, two of which were under age of 15 years. Lesions in 2 (18.2%) patients involved one lobe with unifocal presence. Subpleural lesions were seen in 7 (63.6%) patients. Ground glass opacity (GGO) was the most common sign observed in 7 (63.6%) patients. Crazy-paving pattern and consolidation were detected in 2 (18.2%) and 4 (36.4%) cases, respectively. Based on deep learning quantitative analysis, volume of intrapulmonary lesions on first CT scans was 85.73±84.46 cm^3. In patients with positive findings on CT images, average interval days between positive real-time reverse transcriptase polymerase chain reaction assay and peak volume on CT images were 5.1±3.1 days. In conclusion, typical CT findings can be detected in over 70% of asymptomatic SARS-CoV-2 carriers. It mainly starts as GGO along subpleural regions and bronchi, and absorbs in nearly 5 days.

Introduction

Since the first outbreak in late 2019, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection has dramatically spread throughout the world, and has caused 105 952 deaths in five continents by 12 April 2020 (1). The epidemiologic picture is still on changing on a daily basis. The population is generally susceptible to the SARS-CoV-2. One of the main methods to control spread of the virus is to cut-off transmission routes by isolating susceptible patients from healthy individuals. Identification of the suspected infection in population is urgent and important. World Health Organization suggests that that people with symptoms such as fever, cough and difficulty breathing need seek medical attention (2). However, it is proved that there are asymptomatic carriers of SARS-CoV-2 who can also infect their close contacts (3-5). A study on viral load of asymptomatic patients corroborated this fact by indicating that the viral load detected in one asymptomatic patient was similar to symptomatic patients (6). It is quite difficult to identify the asymptomatic carriers. They can be a covert source of SARS-CoV-2 infection in the community and pose a huge challenge for symptom-management-based control of the disease. Virologic tests on upper respiratory specimens and blood antibody test are the main confirmation methods for diagnosis of SARS-CoV-2 infection. But the capacity of virologic tests is limited by its requirement of high-level facilities and instruments; and time gap between infection and antibody appearance may limit in time identification of high-risk groups. A method that can provide additional diagnostic information is needed to improve our practices. If chest CT imaging, one of the concerned methods in diagnosis and follow-up evaluation of respiratory diseases, have positive findings on asymptomatic carriers is rarely proved.

This retrospective study focuses on chest CT findings of asymptomatic carriers in Beijing, China. We hope to provide a referable CT series on asymptomatic carriers of SARS-CoV-2 for supporting disease control.

Materials and methods

This study was approved by the Ethics Committee of Beijing Ditan Hospital, Capital Medical University (BJDT〔2020〕No. (022)-01). The requirement for informed consent was waived for this retrospective study.

Patients

Records for 267 patients diagnosed with SARS-CoV-2 infection between 24 Jan 2020 and 29 March 2020 in this single center study were retrospectively reviewed (**Fig.1**). Patients with symptoms related to SARS-CoV-2 infection during disease course, including fever, cough, fatigue, muscular soreness, headache, diarrhea, and dyspnea during disease course were excluded. Asymptomatic carriers received nasal or throat swab test for real-time reverse transcriptase polymerase chain reaction (rRT-PCR) of SARS-CoV-2 because they had close contacts with patients who developed symptomatic 2019 Coronavirus disease (COVID-19), based on guidelines published by Chinese general office of the national health commission (7).

CT image acquisition and evaluation

CT images were performed using a Siemens Emotion 16 CT scanner (Siemens Healthineer, Germany). The scanning was set at energy of 130kV and automatic current based on body weight. Images were obtained at 10 mm thickness and 5 mm interval and reconstructed with high spatial resolution algorithm into 1.5mm thickness. The images were interviewed at window settings suitable for assessment of lung parenchyma (window width:1550 HU; window level: –560 HU) and mediastinum (window width:400 HU; window level: 40 HU).

The chest CT images were analyzed qualitatively and quantitatively. The number of affected lobes, distribution, density and shape of intrapulmonary lesions; lung volume loss, pleural effusion and lymphadenopathy in each patient's chest CT images were the main aspects of qualitative analysis. CT signs were described using internationally standard nomenclature defined by the Fleischer Society glossary (8). Lung volume loss was defined as reduced inflation of part of the lung with abnormal displacement of fissures, pleural, bronchi and/or vessels, based on definition of atelectasis by Fleischer Society glossary. Quantitative analysis on the volume of lesions in the chest CT images were analyzed by a pneumonia assisted diagnosis system (PneumoniaDoc, ShuKun Technology Co., Ltd, China), which used deep learning method to automatically identify pneumonia regions on chest CT and quantitatively calculate the volumes.

Statistical analysis

The counting data were presented as the number of cases (percentage of total), and quantitative data were recorded as the mean± standard deviation.

Results

Demographics and laboratory findings

There were 11 persistent asymptomatic patients with SARS-CoV-2 infection enrolled in this study, with an average age of 29.3±13.0 years. All the 11 asymptomatic patients were tested for chest CT scan during the study period. Basic information and laboratory test results were present in **Table 1**. The ratio of men to women was 7:4. All of the patients were hospitalized for observation for 18.5±4.7 (10-28) days after positive rRT-PCR detected. The results of rRT-PCR for SARS-CoV-2 turned negative in 9 patients when discharging from hospital, and still positive in 2 patients (transferred to another institution for quarantine). Analysis of peripheral blood cells revealed normal peripheral leukocyte count and neutrophils count in 9 asymptomatic patients (81.8%). One (9.1%) patient had reduced blood neutrophils; one (9.1%) patient had slightly elevated blood leukocyte and neutrophils. Normal C-reactive protein and erythrocyte sedimentation rate were seen in 9 (81.8%) patients.

Chest CT evaluation

All the patients accepted first chest CT examination in 2.2±1.7 days after positive rRT-PCR for SARS-CoV-2 revealed. Findings on CT images were tabulated in **Table 2**. There were 3 patients

(27.3%) who had normal first chest CT, two of whom were under the age of 15 years. Eight (72.7%) patients had intrapulmonary lesions. The number of affected lobes in patients with pneumonic findings on CT images was 2.5±1.1. Lesions in 2 (18.2%) patients involved one lobe with unifocal presence. The rest 6 (54.5%) patients had multilobular involvement. Subpleural lesions were seen in 7 (63.6%) patients, two of whom accompanied with central lesions (**Fig. 2**). Lesions of 1 (9.1%) patient distributed diffusely (**Fig. 3**). Ground glass opacity (GGO) was the most common sign observed in 7 (63.6%) patients (**Fig. 2, 3**). GGO of five (45.5%) and 4 (36.4%) cases were spherical and patchy, respectively. Thickened interlobular and intralobular septa within GGO were seen in 2 (18.2%) patients, presenting as crazy-paving pattern. Consolidation was detected in 4 (36.4%) patients, three of whom manifested as punctate consolidation in the center of GGO (**Fig. 2**). Stripe was observed in 1 (9.1%) patient. Lung volume loss wasn't seen in this group of patients. No patient with plural effusion and enlarged intrathoracic lymph nodes was noted.

Based on deep learning quantitative analysis (**Fig. 4**), volume of intrapulmonary lesions on first CT scans was 85.73±84.46 cm^3 (listed in **Table 2**). All 11 patients received a second CT scan in 11.4±6.7 days after the first scan. The three (27.3%) patients who had no positive findings in the first examinations still had no lesions in their lungs. Five (45.5%) patients showed improvement. Three (27.3%) cases exhibited slight progression. Four patients had third follow-up CT scan in 7.8±1.8 days after the second scan. Lesions in all the four cases improved. In patients with positive findings on CT images, average interval days between positive rRT-PCR and peak volume on CT images were 5.1±3.1 days. Changes of volume of lesions on follow-up CTs were present in **Fig. 5**.

Discussions

Chest CT imaging is a vital component in the objective evaluation of intrapulmonary lesions in patients with SARS-CoV-2 infection. Since Lei et al. firstly unveiled CT findings of a 33 years old female patient with COVID-2019 on 2020 Jan 31 (9), series studies on medical imaging of

SARS-CoV-2 infection has been conducted and reported. Those studies interpreted that GGO, crazy-paving pattern and consolidation along subpleural region and bronchi were the most common findings in infected patients (9-13). It is reported that 56% to 92.4% of patients had intrapulmonary findings on CT images (10, 11, 14). Compared to RT-PCR assay, 60% to 93% of patients had positive CT before positive RT-PCR results (15, 16). Based on these studies and clinicians' experiences, China, as first high-risk country, had encouraged diagnosis based on clinical and chest CT findings alone in cities with worst outbreak, to better control the infection spread (7). The strategy, accompanied with mobile cabin hospital, leaded to decreased number of newly infected patients. However, till now, the major management strategy of disease control is symptom-based. Limited data are available for asymptomatic infections. Meng et al. conducted a retrospective study on CT features of 58 COVID-19 patients without symptoms onset at admission, providing information on CT evaluation of initiatory asymptomatic patients; however, 16 patients in the studied group presented symptoms after admission (17). Another study by Inui et al. on the large cluster of asymptomatic COVID-19 patients from cruise ship "Diamond Princess" without stated exclusion of pre-symptomatic patients was also published (18). However, recognition of contagious patients who are persistent asymptomatic is more challenging and precise studies on this group of patients are of important value in disease control. In this retrospective study of 11 asymptomatic patients with confirmed SARS-CoV-2 infection, we focus on chest CT findings of the persistent asymptomatic carriers and hope to provide a referable CT series on this group of patients for disease control. It is noteworthy that 8/11 (72.7%) of asymptomatic carriers had intrapulmonary lesions; only 3/11 (27.3%) of carriers had normal CT with complete absence of lesions in the lung, two of whom were children. In a study on clinical characteristics of asymptomatic patients with SARS-CoV-2 infection in China, Hu et al. also suggested that asymptomatic young cases were prone to have a normal CT image (19). In fact, not only in asymptomatic young carriers, but also in young patients with symptoms, value of chest CT in diagnosis of the virus infection is controversial (20). It is reasonable to speculate that the proportion of asymptomatic adult patients with abnormalities on chest CT images is even higher. The proportion is close to that in the study by Meng et al. (100%), but is much higher than that in the study by Inui et al. (54%). Second finding of this work is that in patients with intrapulmonary lesions, spherical or patchy GGOs along subpleural region and bronchi were the most common finding in this group of patients, concurring with early radiology investigative efforts (9-11, 21, 22). This has been considered as the chest CT hallmark of SARS-CoV-2 infection. This pattern of disease, similar to that described in previously outbreak of coronavirus infection such as SARS and MERS (23, 24), reveals initial acute damage along the airway, starting with diffuse alveolar damage and airway inflammation consistent to pathological changes (25). Crazy-paving pattern and consolidation described in previous studies were less likely seen in this group of patients, appeared in 2/11 (18.2%) and 4/11 (36.4%) asymptomatic carriers. In addition, we found lesions in 2 (18.2%) patients were unifocal. It is reported that unifocal lesion present in the early phase and often progressed into multiple lesions in the progressive phase (21). Sign of lung volume loss was absence in this group of patients. According to previous report, lung volume loss is a supportive sign for alveolar collapse, which is commonly seen in severe COVID-19 pneumonia (26). The appearance of unifocal lesion and the absence of signs of lung volume loss suggest that lung lesions are mild, which is consistent with clinical manifestations in asymptomatic patients. Another finding of this work is that intrapulmonary lesions in asymptomatic carriers reach peak volume in approximately 5 days after positive rRT-PCR assay. A work performed by Pan et al. on a series of CT images of 21 patients recovering from mild COVID-19 pneumonia provided a widely accepted time course of lung changes (27). They defined four stages of lung involvement: early stage, progressive stage, peak stage and absorption stage. Maximum lung involved peaked at approximately 10 days. But in asymptomatic carriers, peak stage tends to appear earlier without obvious progression.

In conclusion, typical CT findings can be detected in over 70% of asymptomatic SARS-CoV-2 carriers. It mainly starts as GGO along subpleural regions and bronchi, and absorbs after nearly 5 days. Chest CT can provide extra information on asymptomatic carriers of SARS-CoV-2 for supporting disease control.

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Conflicts of Interest: None to declare.

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Figure 1. Flowchart of this study.

Figure 2. A 51 years old male asymptomatic patient (case 4) with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. Spherical ground glass opacity (GGO) (▲) is found in the subpleural lung field of the left upper lobe, with punctate consolidation in the center (*), accompanied with spherical GGOs (▲) along the bronchial bundle in right upper lobe.

Figure 3. A 48 years old female asymptomatic patient (case 2) with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. The first chest CT scan obtained on day 4 from positive real-time reverse transcriptase polymerase chain reaction (rRT-PCR) shows diffuse ground glass opacity (GGO) in left superior lobe and bilateral lower lobes without predilection to subpleural region or along bronchi.

Figure 4. Application of deep-learning-based pneumonia assisted diagnosis system in quantitative analysis. The program can accurately segment the lesion (red) and calculate the volume of lesions in each lobe. The original CT image shows the lesion (▲) in the posterior basal segment of right lower lobe.

Figure 5. Changes in the volume of intrapulmonary lesions on chest CT from positive real-time reverse transcriptase polymerase chain reaction (rRT-PCR) (in days). Patient 1, Patient 4 and Patient 7 exhibited slight progression on the second CT scan, and showed absorption on the third scan. The rest patients showed no progression after first scan.

Table 1 Detailed demographics and laboratory findings of 11 asymptomatic SARS-CoV-2 carriers

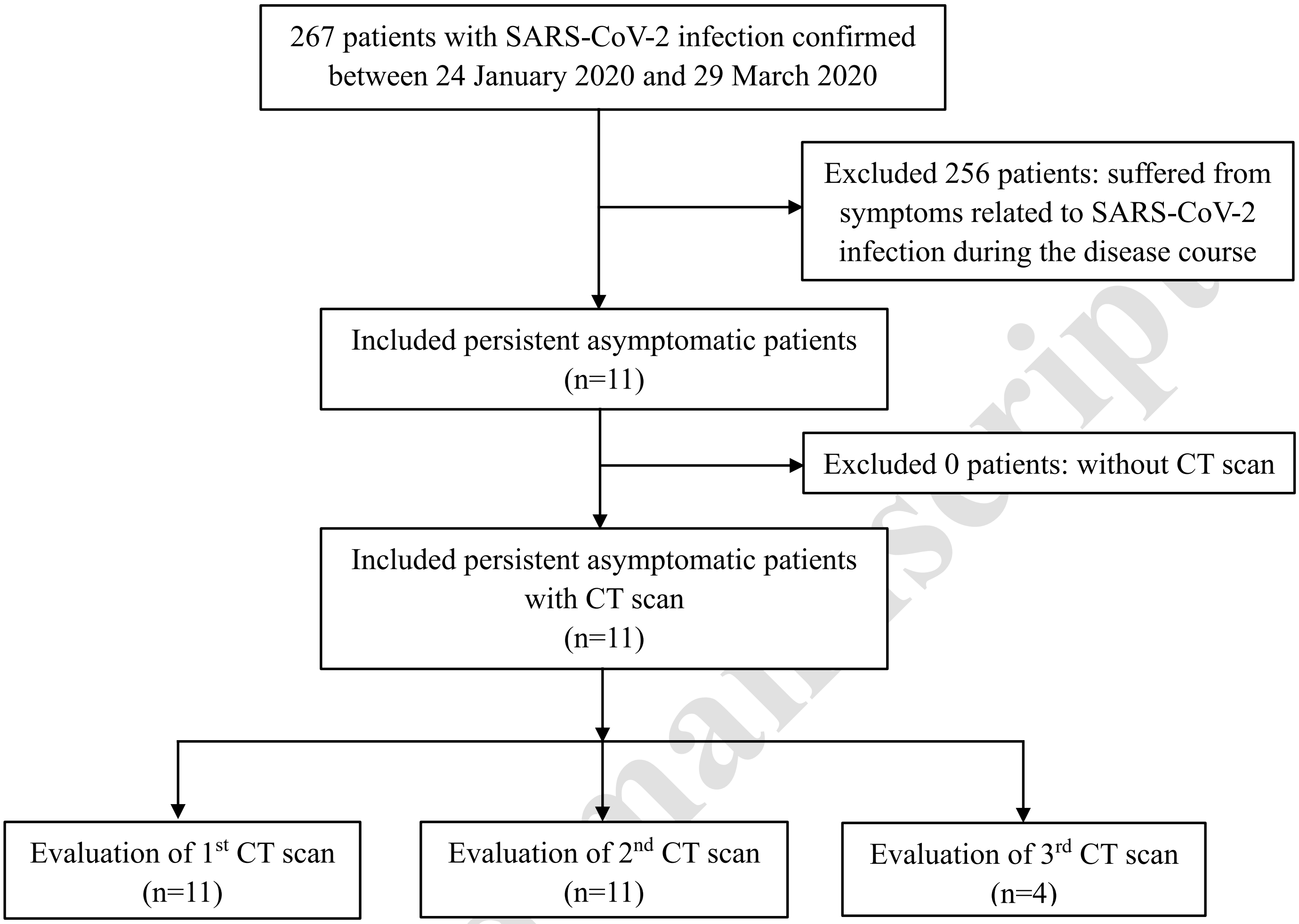
Case	Gender	Age	Peripheral WBC ($4\sim10\times10^9$/L)	Peripheral NEUT# ($2\sim8\times10^9$/L)	Peripheral LYMPH# ($1\sim5\times10^9$/L)	CRP (0~5 mg/L)	ESR (0~20 mm/h)
1	F	36	5.99	2.3	3.06	3.4	31
2	F	48	5.64	4.09	1.23	0.8	23
3	M	50	5.47	3.61	1.45	3.4	18
4	M	52	8.05	5.2	2.16	11.9	10
5	M	32	4.5	2.23	1.97	1.3	18
6	M	23	5.36	3.06	1.63	0	1
7	M	21	5.6	2.5	2.48	0.5	2
8	F	23	12.6	10.7	2.09	0.5	7
9	M	7.3	4.81	1.89	2.64	1.6	5
10	M	6.8	5.68	2.29	2.92	0	1
11	F	23	3.56	1.93	1.1	0.7	10

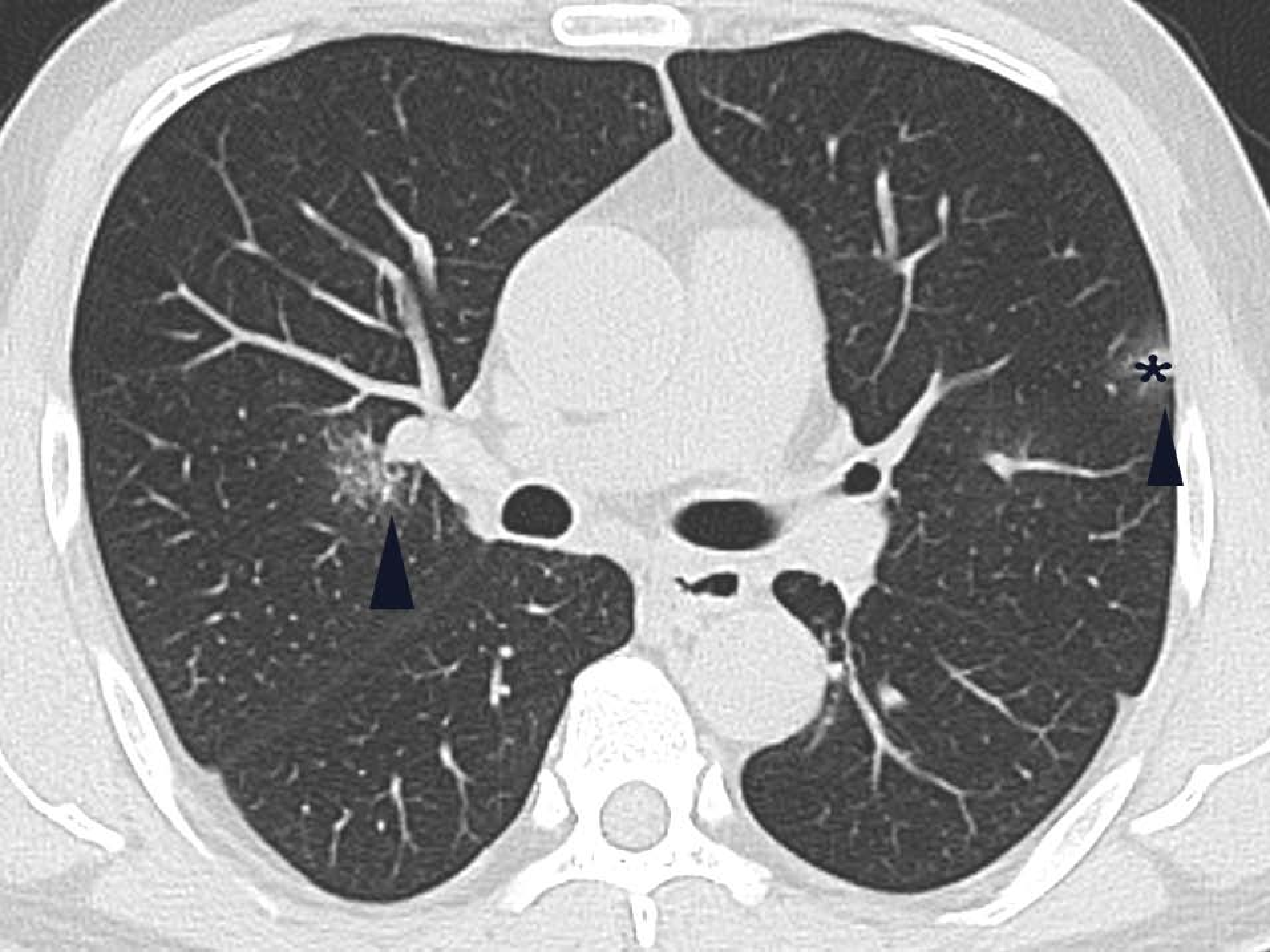
Note: WBC: white blood cells count; NEUT#: neutrophils count; LYMPH#: lymphocyte count; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate.

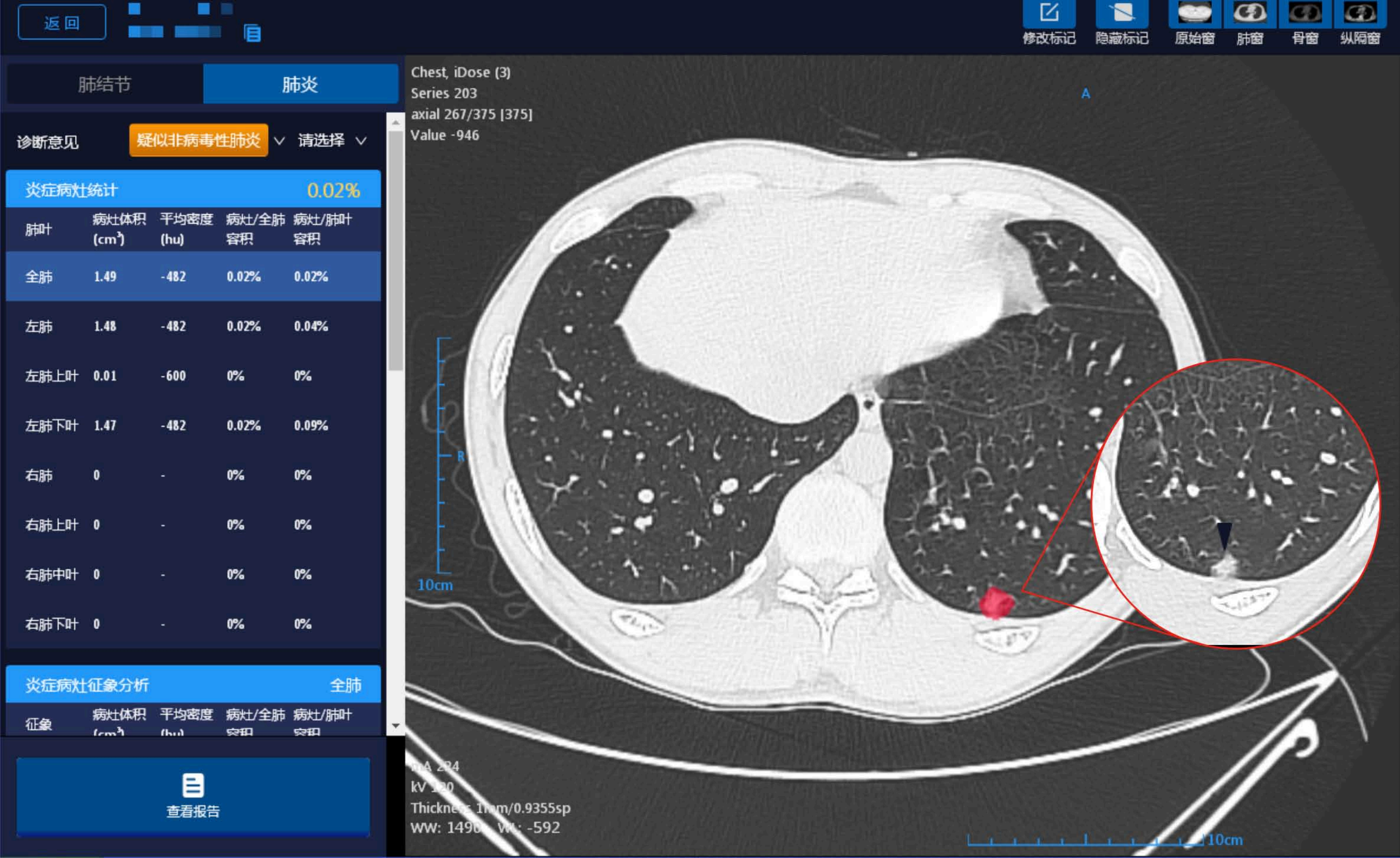
Table 2 Chest CT findings of 11 asymptomatic SARS-CoV-2 carriers

Case	No. of lobes	GGO*	Crazy-paving pattern*	Consolidation*	Lung volume loss*	plural effusion*	Lymph nodes*	Deep-learning-based quantitative lesion volume (cm^3)		
								1st CT scan	2nd CT scan	3rd CT scan
1	2	1	0	0	0	0	0	68.86	91.78	75.44
2	5	1	1	0	0	0	0	360.25	133.87	45.55
3	3	1	1	0	0	0	0	149.05	27.11	null
4	4	1	0	1	0	0	0	22.32	60.04	18.22
5	2	1	0	0	0	0	0	0.26	0.23	null
6	2	0	0	1	0	0	0	82.16	48.89	null
7	1	1	0	1	0	0	0	1.67	31.33	20.18
8	1	1	0	1	0	0	0	1.27	0.8	null
9	0	0	0	0	0	0	0	0	0	null
10	0	0	0	0	0	0	0	0	0	null
11	0	0	0	0	0	0	0	0	0	null

Note: Value 0 in * marked column refers to absence of relevant signs; value 1 refers to presence of signs. GGO: ground glass opacity.


267 patients with SARS-CoV-2 infection confirmed between 24 January 2020 and 29 March 2020
Excluded 256 patients: suffered from symptoms related to SARS-CoV-2 infection during the disease course
Included persistent asymptomatic patients (n=11)
Excluded 0 patients: without CT scan
Included persistent asymptomatic patients with CT scan (n=11)
Evaluation of 1st CT scan (n=11)
Evaluation of 2nd CT scan (n=11)
Evaluation of 3rd CT scan (n=4)





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疑似非病毒性肺炎
请选择
炎症病灶统计 0.02%
肺叶 | 病灶体积(cm³) | 平均密度(hu) | 病灶/全肺容积 | 病灶/肺叶容积
全肺 1.49 -482 0.02% 0.02%
左肺 1.48 -482 0.02% 0.04%
左肺上叶 0.01 -600 0% 0%
左肺下叶 1.47 -482 0.02% 0.09%
右肺 0 - 0% 0%
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炎症病灶征象分析 全肺
征象 | 病灶体积(cm³) | 平均密度(hu) | 病灶/全肺容积 | 病灶/肺叶容积
查看报告
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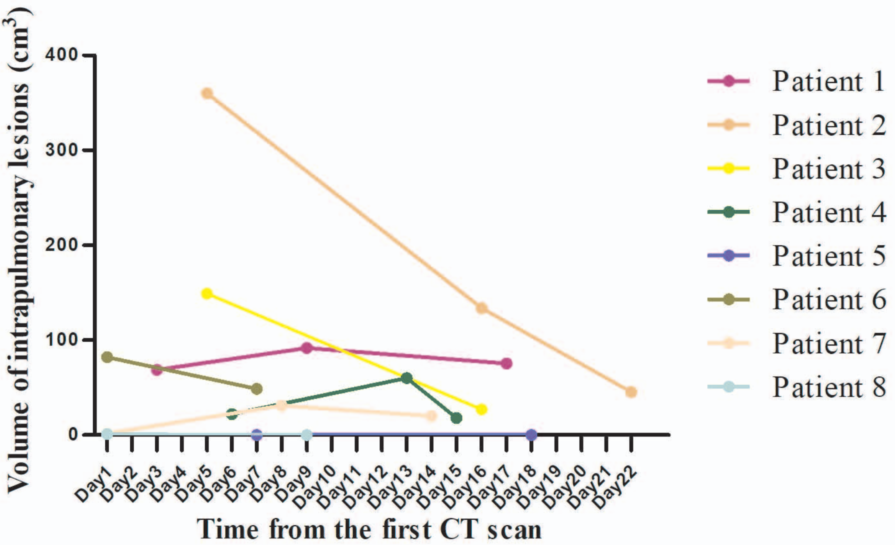
Volume of intrapulmonary lesions (cm³)
400
300
200
100
0
Day1
Day2
Day3
Day4
Day5
Day6
Day7
Day8
Day9
Day10
Day11
Day12
Day13
Day14
Day15
Day16
Day17
Day18
Day19
Day20
Day21
Day22
Time from the first CT scan
Patient 1
Patient 2
Patient 3
Patient 4
Patient 5
Patient 6
Patient 7
Patient 8