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# Computed Tomography (CT) algorithm follow-up and nodule management

The suggested algorithm for nodule follow-up and diagnostic procedures are shown in figure S1. The consistency of the nodule was defined as solid if the nodule obscured the entire lung parenchyma, partly solid if it obscured part of the lung parenchyma, and nonsolid if it obscured none of the parenchyma. If the result on CT was positive, the type of workup depended on the diameter of the largest nodule. For nodules 5 to 14 mm in diameter, the suggested option was to perform another chest CT at 3 months; if the images showed growth of the nodule, defined as at least a 10% increase, then biopsy, ideally by fine-needle aspiration, was to be performed. If there was no growth, we suggested a follow up chest CT at 6, 12 and 24 months. Significant nodule decrease was defined as a reduction in diameter of at least 10%. Subjects underwent diagnostic measures if nodules significantly increased on any follow-up CT. For nodules 15 mm in diameter or larger (whether solid, partly solid, or nonsolid), two options were offered, immediate biopsy or a control chest CT 3 months later with a biopsy in case of significant increase in the diameter in the latter CT.

In case of a nodule compatible with lung infection, we suggested a new CT at least 4 weeks after a 7 to 10 days antibiotic course, and if no resolution or growth of nodule was observed, biopsy or CT follow up was to be performed. Other exams, such as positron-emission tomography (PET), were left to the decision of each clinical center. If no significant nodule was visualized on baseline chest CT, no ulterior CT was programmed. Each radiologist collected on a standardized chest CT report the sizes and localization of significant images visualized on the baseline and follow up chest CT. Lung cancer biopsies were done by bronchoscopy if the nodule was in the bronchus or near the bronchus or by chest CT guided fine-needle biopsy. If necessary, surgical biopsy could be proposed. All subjects were followed up until their final visit planned two years after study inclusion.

eFigure 1 lung nodule detection and diagnostic work up algorithm. CT: Computed Tomography. M: month.

# Additional description of nodules and evolution

A total of 133 positive images were described in 88 subjects: 118 were solid nodules, 8 non-solid nodules, 3 positive adenopathies and 4 endobronchial images. Description of the 118 solid nodules showed that 78 (69%) had a diameter between 5 and less than 8 mm, 31 (26%) between 8 and less than 15 mm and 9 (8%) of 15 mm or more. Ten (8%) of the 126 solid or non solid nodules increased in size between baseline and the last realized chest CT, of which 3 were lung cancers and one a *Mycobacterium Xenopi* granulomatous infection. Sixty-nine (55%) nodules remained stable after a time lapse of more than 3 months, of which one was a lung cancer and one a mucosa-associated lymphoid tissue (MALT) lymphoma. Thirty-one (25%) nodules had significantly diminished. Eleven (9%) significant nodules (in 8 subjects) were not furthermore evaluated, one of which was a lung cancer, as described in the following paragraph (case 49013). Five nodules had been previously visualized on diagnostic CT archives in clinical centres, were considered stable with thus no indication of a biopsy. Two nodules were immediately biopsied in two subjects after first CT, and 3 nodules had not been followed in 2 deceased subjects and one lost to follow up.

Of the 94 subjects with significant images, 67 subjects (71%) had one, 18 subjects (19%) had 2 and 9 subjects (10%) had 3 or more significant images.

# Number of additional radiological procedures, other than planned protocol CT

Sixty-one complementary radiological procedures were engendered by the discovery of abnormalities on study chest CT. Amongst these, 12 were positron emission tomography scans, 10 were additional diagnostic chest CT, 5 were abdominal scans and 6 were cerebral scans.

# Detailed report of two subjects with delayed procedures:

Subject 67003 had a baseline chest CT showing a solid nodule of 13 mm located next to a cavitary cyst in the superior right pulmonary lobe. She underwent fine needle chest CT biopsy as the nodule had significantly increased in diameter on CT follow up, but histological analysis only revealed inflammatory cells. Four months after the biopsy, a symptomatic stage IV lung adenocarcinoma was diagnosed, with cerebral and right adrenal gland localizations.

Subject 49013 had a speculated 10 mm solid nodule visualized in the left superior lobe on baseline chest LDCT, and the subject was referred to a pneumologist. Unfortunately, the medical appointment was missed and he was seen one year later with a left parietal thoracic pain symptomatic of an apical pulmonary mass with D1-D2 and D2-D3 intervertebral foramina invasion.