**Supplementary text:**

# Screening for Interstitial Lung Disease in Systemic Sclerosis: Performance of High-resolution Computed Tomography with Limited Number of Slices - a Prospective Study

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## Definition of ILD

ILD was defined as present if at least one of the following findings was found: ground-glass opacities, sub-pleural reticulation with or without pleural irregularities, traction bronchiectasis and/or honeycombing. Scars and band-like changes typical for earlier infection were not considered as ILD. In our study protocol we also excluded cystic lesions other than honeycombing, although they can be associated with ILD, because there are only few case reports and no correlation between cystic lung changes and SSc.

## Limitations of the study

As stated, the new protocol does not allow assessing lymph nodes comprehensively and cannot depict lung nodules outside the slices. If there is a clinical suspicion and a need to image lymphadenopathy or lung nodules, then a regular CT is mandatory. In this study, 10 patients had a lung nodule that needed a follow-up. All nodules were less than 6 mm in diameter. Based on the Fleischner Guidelines a follow-up exam was performed, and all nodules were stable [1]. Only 2 nodules where not seen on the reduced scan, while the other 8 nodules were detected in the reduced scan. 2 other cases had dystelectasis, which both were recognized also on reduced CT. Lymphadenopathy was present in 12 patients on standard CT. All cases of moderate lymphadenopathy (N=5, defined as 3 or more lymph nodes with short-axis exceeding 1 cm) were also visible in the reduced CT. Mild lymphadenopathy (N=7, defined as presence of 1 or 2 lymph nodes with short axis exceeding 1 cm) was detectable in 3/7 cases on the reduced CT.

Another limitation is the fact that only one reader reviewed the standard CT's. To overcome the problem of possible misclassification due to reader issue, a training session was performed on non-study related cases to harmonize and optimize assessment and to reduce variability. This session ensured that all readers are using the same definition for ILD. Indeed, the inter-reader agreement was very high after the training session (for detection of ILD: κ = 0.76; for extend of ILD: κ = 0.73).

**CT and radiation risk**

The natural background dose is about 3 to 6 mSv depending on the level above sea and the Radon exposure. The CT brings an additional dose to this background dose. Notably, the background dose is disposed over a year over the entire body, giving the DNA time to repair, whereas the CT-dose is provided in 5 seconds and only over the chest.

In medical practice, it is important that the patients' exposure to radiation is as low as possible. During the last years, focus has been set on the cumulative radiation dose, which is a highly relevant issue when discussing harm of CT-based screening, e.g. for lung cancer.

The radiation risk at high doses > 50 mSv is well established from atomic bomb data and an increasing number of clinical studies. We know that in the age group screened (> 50 years), the risk for lung cancer induction is higher than the risk of induction of any other cancer [2]. In the range between 5 and 50 mSv, only estimates can be made; usually a linear extrapolation to 0 is performed. Using this linear non-threshold theory, the life-time attributable cancer risk at age 60 and exposure to 1 mSv is calculated to be 1 in 20,000 [3-5].

Bach et al. [6] estimated that participants from the National Lung Screening Trial (NLST) received approximately 8 mSv per participant over 3 years. Estimates of harms from such radiation come from several official bodies and commissioned studies, based on dose extrapolations from atomic bombings and also many studies of medical imaging [2]. Using the NLST data, these models predict that approximately 1 cancer death may be caused by radiation from imaging per 2500 persons screened. Another paper by Brenner suggest that a single baseline CT screening examination for lung cancer using a low dose protocol would results in a fairly low risk (<0.06%) for radiation-induced lung cancer, and negligible risk for other cancer [7]. However, with annual screening the radiation exposure from annual CT lung examinations could increase the number of additional tumors by approximately 1.8% [7]. With regard to potential additional diagnostic studies for follow-up McCunney et al. calculated that the radiation exposure from low-dose CT and follow-up procedures exceed life-time radiation exposure among nuclear power workers and atomic bomb survivors [8]. The CT-dose needed to depict subtle ILD changes is higher than for a node, as image noise needs to lower.

In conclusion, although all these numbers are based on calculations and assumptions, there are solid grounds for an increased risk of radiation-induced lung cancer in patients who undergo repeated CT examinations. Therefore, especially in the case of patients who require yearly CT follow-up, the relevance of reducing the radiation risk by a reduced CT scan as the one presented in our study might indeed outweigh the eventual risk of missing additional incidental findings.

**References:**


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