Joint Statement of the German Radiological Society and the German Respiratory Society on a Quality-Assured Early Detection Program for Lung Cancer with Low-Dose CT*

Positionspapier der Deutschen Röntgengesellschaft und der Deutschen Gesellschaft für Pneumologie und Beatmungsmedizin zu einem qualitätsgesicherten Früherkennungsprogramm des Lungenkarzinoms mittels Niedrigdosis-CT

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ABSTRACT

Substantial new data on the early detection of lung cancer with low-dose CT has become available since the last joint statement of the German Radiological Society and the German Respiratory Society was published in 2011. The German S3 guideline on lung cancer was revised in 2018 and now contains a weak recommendation regarding the early detection of lung cancer with low-dose CT in a quality-assured early detection program. These new developments required a change in the position of the involved professional societies. This joint statement describes the main features of a quality-assured program for the early detection of lung cancer with low-dose CT in Germany.

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Key points:

- New study data on early detection of lung cancer with low-dose CT and the new German S3 guideline on lung cancer required a new positioning of the involved professional societies.
- The involved professional societies strongly recommend that low-dose CT examinations for early detection of lung cancer should only be performed within a quality-assured program.
- The article describes some fundamentals of such a quality-assured early detection program.

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ZUSAMMENFASSUNG

Seit dem letzten gemeinsamen Positionspapier der Deutschen Röntgengesellschaft und der Deutschen Gesellschaft für Pneumologie und Beatmungsmedizin im Jahr 2011 hat sich die Datenlage zur Lungenkrebsfrüherkennung mit Niedrigdosis-CT deutlich erweitert, und in der 2018 revidierten S3-Leitlinie Lungenkarzinom wird eine schwache Empfehlung zur Lungenkrebsfrüherkennung mit Niedrigdosis-CT in einem qualitätsgesicherten Früherkennungsprogramm ausgesprochen. Diese neuen Entwicklungen erforderten eine Neupositionierung der beteiligten Fachgesellschaften. Das vorliegende Positionspapier beschreibt Grundzüge eines qualitätsgesicherten Früherkennungsprogramms für Lungenkrebs in Deutschland.

Background

In January 2018, the involved professional societies adopted the revised S3 guideline on lung cancer [1]. It includes for the first time a weak recommendation regarding the early detection of lung cancer with low-dose CT (as soon as the relevant legal bases exist) in

- asymptomatic persons at risk between 55 and 74 years of age and with a history of ≥ 30 years of smoking and fewer than 15 years since smoking cessation, and
- asymptomatic persons at risk who are at least 50 years old and have a history of ≥ 20 years of smoking and one of the following additional risk factors: history of lung cancer, positive family history for lung cancer, history of malignant ENT tumor or another malignant tumor associated with smoking, history of lymphoma, exposure to asbestos, COPD or pulmonary fibrosis.

This early detection is to be performed under the following conditions:

- Multidisciplinary treatment team including at minimum specialists from the fields of radiology, pulmonology, thoracic surgery, oncology, and radiotherapy, ideally at a certified lung cancer center;
- Concomitant smoking cessation;
- Continuous documentation and comparison of findings;
- As part of a quality-assured early detection program.

This recommendation is based on a reevaluation of the currently available studies on the early detection of lung cancer with low-dose CT. Subgroup analyses of the American National Lung Screening Trial (NLST) that have since been published showed a strong positive correlation between the individual lung cancer risk and the effectiveness of lung cancer screening. In the quintile of study participants with the highest lung cancer risk, 12 lung cancer deaths per 10 000 person years were prevented while the value in the quintile with the lowest risk was only 0.2 [2]. This can explain the negative results of the European screening studies published at the time of the guideline revision. Compared to the NLST, these studies had milder inclusion criteria (15 to 20 pack years versus 30 pack years in the NLST) and also a significantly smaller number of cases (1186 to 2052 in the study arm per study versus over 26 722 in the study arm of the NLST).

In the pooled data of the two Italian studies (DANTE and MILD), there was an 11 % lower overall mortality rate in the screening arm of the study with a longer follow-up period. However, this was not statistically significant [3].

After the S3 guideline on lung cancer was published, the results of two randomized European screening studies were published and these results support the main statements of the NLST. The results of the Dutch-Belgian NELSON study, which are currently only available as an abstract, show a lung cancer mortality rate that is 26 % lower in men and 39–61 % in women in the screening arm [4]. Moreover, the German LUSI study including 50- to 69-year-old smokers with at least 25 years of smoking found a significant reduction of the lung cancer mortality rate of 69 % in women in the screening arm, while no reduction in the lung cancer mortality rate could be detected in men [5].

The German Radiological Society and the German Respiratory Society feel that the S3 guideline requirement that early detection examinations only be performed as part of a quality-assured early detection program should be strongly supported. Such a program should be made accessible to all persons in Germany with a corresponding risk profile and replace examinations currently performed outside of a quality-assured early detection program. The present position paper was written to describe the basic elements of a possible early detection program as partially defined by the S3 guideline.

Basic conditions for early detection examinations

A decisive factor in the success of an early detection program is timely and appropriate workup and treatment in the case of positive findings. The S3 guideline requires a multidisciplinary treatment team (specialists in radiology, pulmonology, thoracic surgery, oncology, radiation therapy), ideally at a lung cancer center certified by the German Cancer Society and at the sites of their contractual partners.

It can be assumed that a certified lung cancer center possesses the necessary qualifications for a diagnostic workup. Further suitable centers are oncology centers certified by the German Cancer Society and specialized in lung cancer. Such centers are referred to in the following as treatment centers.

Diagnostic workup in the case of positive screening findings is to be performed at these centers. The actual early detection examinations, i. e., informed consent discussions and low-dose CT examinations, are performed at the treatment center or alternatively at outpatient or inpatient radiology institutions that are contractual partners of the treatment centers. To ensure the appropriate structural and process quality, these centers should meet the following requirements:

- Cooperation agreements with a treatment center are to be concluded to ensure that low-dose CT findings suspicious for cancer are presented at the treatment center and recommendations for the further course of action are determined on a multidisciplinary basis, for example as part of a tumor board review at the treatment center. The cooperation agreement is to include a description of a structured procedure for the workup of positive findings in accordance with the guideline.
- As a result of the cooperation with a suitable center, all participants of the early detection program are offered participation in a smoking cessation program.
- Suitable examination protocols for low-dose chest CT (as described in section 4) are implemented on the CT scanner.
- The radiology institution is accredited for participation in the early detection program, for example by the German Radiological Society. The requirements stated above are reviewed during the accreditation process. Accredited centers are given access to software. The functionality of this software is described in greater detail in section 5. The software allows the evaluation of findings including CAD analysis as a second reader, standardized volumetry (same software for all involved radiology institutions) and recording of the participant and his findings in a central database. At the same time, this allows follow-up of abnormal findings from previous examinations at various radiology institutions.

The required qualifications of radiologists participating in the early detection program which exceed specialist status with respect to radiation protection expertise and specific diagnostic knowledge (e. g. regarding types of early lung cancer and standardized reporting) must be defined in cooperation with the professional societies.

Inclusion of participants in the early detection program and informed consent discussion

Pulmonologists who provide inpatient or outpatient care and are contacted by persons with an elevated lung cancer risk play the key role in determining who will be included in the early detection program. In this initial meeting, the pulmonologist provides counseling and reviews the inclusion criteria. The possibility of smoking cessation as the most effective measure for reducing the risk of lung cancer should also be discussed.

To achieve optimal effectiveness of the early detection program, the individual lung cancer risk must be assessed using risk models. The resulting inclusion criteria for the early detection program must still be developed by the professional societies.

The pulmonologist is responsible for coordinating the early detection process. The pulmonologist reviews the inclusion criteria, makes the referral to the radiologist, is informed of the CT results, informs the participant of the early detection program, and initiates any necessary additional examinations for diagnostic workup in the case of positive findings.

In radiology every participant of the early detection program is informed in writing of the risks associated with the early detection examination. The following risks in particular must be presented:

- Risk of radiation-induced tumor as a result of low-dose CT;
- Frequency of false-positive findings of the early detection examination and the associated consequences, ranging from unnecessary stress and additional follow-up to invasive workup of benign findings;
- Remaining risk of developing incurable lung cancer despite regular early detection examinations;
- Possibility of detecting lung cancer that would not have caused any symptoms over the course of the participant's life (overdiagnosis).

CT examination technique and reporting of findings

The low-dose CT examination parameters should be sufficiently adapted to the constitution of the person to be examined to ensure the ALARA (as low as reasonably achievable) principle of radiation protection while avoiding non-diagnostic examinations in overweight patients. Therefore, excellent protocol recommendations for chest CT using the low-dose technique were recently developed and published by the working group for the use of diagnostic radiology in work-related and environmental diseases (AG DRauE) of the German Radiological Society [6].

On this basis, suitable low-dose CT examination protocols for lung cancer early detection are developed and regularly updated by the chest working group of the German Radiological Society. This is intended to optimize the risk-benefit ratio under consideration of the installed equipment base and new technical developments.

Any prior examinations are to be made available when findings are reported. Findings are reported in the form of a standardized

written report in which all relevant abnormalities are described and evaluated. The report includes any recommendations regarding follow-up or further workup. Moreover, findings are documented using software suitable for the early detection of lung cancer, including volumetry in the case of solid nodules, with specification of the largest diameter of the ground glass portion and – if present – the solid portion and the volumetry of the solid portion in the case of subsolid nodules. In the follow-up of solid nodules, the volume doubling time should also be determined and documented so that it can be provided to the treatment center to assist in decisions regarding recommendations for the further course of action.

Findings including the necessity for follow-ups and further diagnostic workup should be evaluated in a standardized manner in the early detection program on the basis of the probability of malignancy. In particular, the current version of the Lung-RADS™ developed by the American College of Radiology [7] is suitable for this purpose and is specifically adjusted to the pretest probabilities in a screening population.

Taking into account the limited sensitivity of the radiologist for the detection of small lung cancers using low-dose CT, double reporting either by a second radiologist or by a suitable computer-aided detection (CAD) system is required.

The finding is provided to the referring pulmonologist and in a simplified form to the patient.

Data requirements

Preliminary remark: All steps presented in this section must be able to be implemented in compliance with data privacy laws.

All participants in the early detection program, positive findings, and diagnostic workup results must be recorded in a central database (register). This makes it possible to use early detection program data for observational studies. For research purposes, the data from the early detection program can be combined with existing clinical cancer registers containing data regarding stages, treatments, and survival rates of cases of lung cancer diagnosed in the early detection program.

It is to be expected that participants in the early detection program will not always be able to undergo follow-up examinations at the same radiology institution. Therefore, easy exchange of CT image data and prior findings between radiology institutions participating in the early detection program must be ensured. The results of volumetric measurements of nodules are highly dependent on the volumetry software being used. Use of standardized volumetry software in the early detection program is therefore highly desirable but is difficult to achieve without a central solution that is mandatory for all involved radiology institutions.

A centrally managed IT solution with at least the following functionalities is needed:

- Central processing of participant data, examination findings and recommendations regarding follow-up intervals or diagnostic workup;
- Documentation of the patient informed consent and medical history (risk factors, pack years)
- Graphical user interface for reporting of findings with documentation option for double reporting, volumetry and computer-aided detection (CAD) functionality.
- Generation of standardized reports with recommendation for further course of action based on standardized us of recommendations like Lung-RADS (follow-up interval, diagnostic workup)
- Monitoring of timely implementation of follow-ups needed based on the findings;
- Ability to exchange image data from prior CT examinations between participating radiology institutions;
- Interface for scientific evaluation of data acquired in the early detection program;
- Central documentation of the radiation dose and CT scanner for every CT examination in the early detection program.

Commercially available software solutions should be reviewed with respect to suitability and possible expandability.

Financing of the early detection program

The early detection program must be financed by the cost carriers of the health care sector. This requires a positive benefit assessment by the Federal Joint Committee. In the future the term for this following approval of an early detection procedure by the Federal Ministry for the Environment, Nature Conservation and Nuclear Safety will be reduced to 18 months.

The introduction of corresponding coding options in service and billing catalogs for the documentation of services rendered and their reimbursement is necessary and must be clarified with the cost carriers.

The presentation and clarification of positive early detection findings at the treatment center are services that are currently already covered by statutory and private cost carriers since such services involve the clarification of findings suspicious for malignancy.

A central database and standardized software play a key role in the described early detection program for ensuring complete recording of participants and their findings over time and the standardized documentation of findings. The financing of the central system components has not yet been clarified. In the case of solutions based on a server-client concept, it is conceivable to finance the software on the client side at radiology institutions using for example a pay-per-use model which requires corresponding reimbursement. The financing must be clarified by the time the early detection program is initiated in order to ensure functioning quality assurance since complete recording of all participants and their findings cannot be ensured if a central system is not available when the early detection program is introduced.

Conclusion and outlook

Thanks to the revised S3 guideline on lung cancer and the new Radiation Protection Law, there is now a realistic chance of introducing lung cancer early detection with low-dose CT for persons

at risk in Germany. This requires on the one hand a positive scientific assessment of the method by the Federal Office for Radiation Protection and the subsequent issue of an ordinance by the Federal Ministry for the Environment, Nature Conservation and Nuclear Safety in accordance with § 84 of the Radiation Protection Law and on the other hand establishment of a financing option for the early detection program by the Federal Joint Committee.

The present position paper of the German Radiological Society and the German Respiratory Society describes the basic elements required by the S3 guideline for a quality-assured early detection program. The presented requirements regarding structural and process quality must still be refined during the development of the early detection program and can be expanded to include elements of result quality.

Conflict of Interest

The authors declare that they have no conflict of interest.

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