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Low-Dose CT Screening [LDCT] is Optimal for Lung Cancer Screening; Chest X-Ray Radiograph [CXR] Lacks the Image Information Necessary to Detect Early Lung Cancer

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1. Abstract

1.1. Background: Although lung cancer screening is quite widespread in Japan, the mortality rate from lung cancer continues to be low. The cause lies in the current testing methods for lung cancer screening, which makes it difficult to detect lung cancer at an early stage. Even if lung cancer is discovered, it is often already advanced to the point where good treatment effects cannot be expected. [1] . The CXR method currently used in Japan has been determined to be ineffective in reducing lung cancer mortality in the United States and Europe [2] and is no longer used for lung cancer screening. The reason why this is still used in Japan is that the Japan Lung Cancer Society's Screening Method Review Committee persistently insists that it should be used in local lung cancer screening, stating that ``the effectiveness of the CXR method has been proven in case-control studies.'' This is because society follows suit [3]. This is because screening methods have been decided ahead of time, and whether or not this has led to a decline in lung cancer mortality has not been thoroughly verified [4]. In the United States, the CXR method is no longer used because studies such as the Mayo lung project [2] have led to the firm conclusion that the effectiveness of CXR screening has not been proven, and society has already followed suit [Five]. However, I cannot fully agree with the US move. It is appropriate that the lung cancer screening method in the United States was changed from CXR screening to LD CT screening, but in introducing LDCT screening as a result, it was important to limit those who could undergo the screening to heavy smokers, considered inappropriate [4-6]. While seeking medical information to address problems in chest radiographic imaging, which is my main field of research, and to establish an appropriate lung cancer screening test method, I also sought to determine the appropriate demographic of test takers [selection of test takers; age, We conducted a demonstration experiment on lung cancer screening to collect information such as gender differences, smoking history], noteworthy CT findings in LDCT screening, and appropriate intervals for annual screening [smoking history, age, gender] [7] . We would like to briefly introduce the results to test takers and those involved in formulating screening plans. The Lung Cancer Society's Screening Imaging Review Committee, which cannot publish this kind of information, appears to be focusing on the wrong area.

1.2. How to Carry Out a Demonstration Experiment: The usefulness of low-dose CT screening for lung cancer [LDCT] is described based on the results of a demonstration experiment in Nagano Prefecture. The first experiment (at the time, Matsumoto Research Center) This is a report on a total of 9 years of demonstration experiments, including a 4-year period starting in 1996 [4], followed by a 5-year period experiment conducted at Azumi General Hospital [formerly known as the Hub Station] [7-11].

1.3. Purpose: The purpose of lung cancer screening should be considered as ``early detection of lung cancer.'' This is where the international recognition lies, and the people involved in formulating the screening law at the Japanese Lung Cancer Society are

misguided, as stated above. This article describes the surprising usefulness of LDCT screening and the ineffectiveness of CXR screening, which has traditionally been carried out by the government. Our country's lung cancer screening laws are misguided decisions made by arbitrary or irresponsible people that are not based on medical data. These are the leaders of lung cancer screening who ignore the invalidity of CXR, which I would like to emphasize in this article. Therefore, it is a very embarrassing situation internationally. They probably don't think about the need for early detection of lung cancer.

1.4. Person in Charge of Demonstration Experiment [Initial Experiment]: The main researchers were Shusuke Sone and other doctors, engineers, and administrative staff members of Shinshu University's Department of Radiology and Central Radiology Department at the time, and the research collaborators were the Matsumoto Research Center. researchers and research assistants, as well as medical associations in Shiochiku, Azumino City, some towns and villages in the Okita district, and Suwa District within the prefecture [4].

1.5. Person in Charge [Long-Term Experiment]: The person in charge of the next long-term demonstration experiment was Shusuke Sone, who was transferred to Azumi General Hospital [former name] and conducted the experiment with the cooperation of the hospital's respiratory disease-related staff [9].

1.6. Permission from the Ethics Committee: Both experiments were conducted with permission from the ethics committee. The first demonstration experiment was conducted for four years starting in 1996 under the approval of the Ethics Committee, chaired by the prefectural medical president at the time.

The following follow-up experiments were conducted under the approval of the Ethics Committee of Azumi General Hospital [formerly known as Azumi General Hospital] [7-9].

1.7. Radiation Dose to Examinees During Medical Examinations: The X-ray tube current was set at 50 mA for the first low-dose CT scan in 1996. In longitudinal experiments, it was determined that the dose could be reduced based on the image quality of the initial CT scan, and the dose was reduced to 25 mA after 1997 [4,6].

1.8. LDCT Implementation Area: The first experiment was conducted in the desired local government in Nagano Prefecture for those who wanted to undergo the LDCT examination. The experimental hub center was set up in an empty hospital room at Shinshu University Hospital in Matsumoto City.

1.9. Long-Term LDCT Implementation Area: Shusuke Sone was transferred to Azumi General Hospital [Ikeda Town, Nagano Prefecture] for five years starting in 2001, and the LDCT was implemented after the appointment of respiratory surgeon Takaomi Hanaoka. The subjects were people who had undergone a complete medical checkup at the same hospital and who wanted to undergo an LDCT examination.

1.10. Publication of Research Results: The first round of experiments at the Matsumoto Research Center was completed in 1998, and the results were submitted and published in the Lancet in the same year. The subjects were 5,483 men and women aged 40-74 [smoking history not confirmed], and the number of lung cancers detected by LDCT was approximately 11 times that of CXR [long-term lung cancer detection rate: large in the first year of screening, but even larger in the following year]. [1996; 22/5483=0.40%, 1997; 25/4425=0.56%, 1998; 9/3878=0.23%] [4,6].

1.11. Comparison with Other Studies: For comparison with LDCT screening, CXR screening was used in conjunction with initial LDCT screening. The number of lung cancers detected by CXR in the first year was extremely low. [The number of lung cancers detected by LDCT /number of patients tested was 0.40%, and 0.03-0.05% by CXR, and the number detected by the latter [CXR] was almost the same as the number [rate] of lung cancer deaths in the region. However, 10 out of 11 cases of lung cancer detected by LDCT are present but not detected by CXR, resulting in false negative cases] [4].

1.12. Results of Long-Term Demonstration Experiments: Tests at JA Nagano Azumi General Hospital were compiled mainly for the shape of tumor shadows and semi-automatic measurement of tumor shadows [7-11].

In the main text, the author provided a tentative definition of early-stage lung cancer and, based on demonstration experiments, sought a screening method that would pass this definition. We then compared LDCT screening with CXR screening. If a successful screening method is implemented correctly, the 5-year post-operative survival rate [5-year survival rate] of patients detected by screening should approach 100% [7-10]. The prognosis with CXR, which makes it difficult to detect early lung cancer, was dismal. On the other hand, in two [unadjusted] demonstration experiments of LDCT screening conducted in Nagano Prefecture, the five-birth rate reached over 90% in both cases. This is a fact. The tumor volume doubling time (TVDT) (Table 1) has also been calculated and published by age and smoking history of the examinee. Although the use of TVDT for screening will be omitted in the main text, we hope that relevant data from local government health officials will be referenced and taken into consideration for appropriate use and implementation of lung cancer screening [9-11].

Table 1: TVDT Values According to the Smoking Status, Age Group and Histology

	n (%)	Mean	TVDT, Number of Patients (percentage)						
			VS*	SI*	S2*	S3*	M*	L*	el.*
All cancers	69 (100%)	459 days	4 (6)	15 (22)	5 (7)	7 (10)	19 (28)	14 (20)	5(7)
Smoking status									
Smokers	42 (100)	364	(10)	(31)	(10)	(7)	(26)	(12)	(5)
current-smokers	28 (100)	453	(11)	(32)	(7)	(7)	(18)	(18)	(7)
ex-smokers	14 (100)	187	(7)	(29)	(14)	(7)	(43)	(0)	(0)
Non-smokers	27 (100)	606	(0)	(7)	(4)	(15)	(30)	(33)	(11)
passive-smokers	9 (100)	871	(0)	(0)	(0)	(11)	(33)	(33)	(22)
non-smokers	18 (100)	473	(0)	(11)	(6)	(17)	(28)	(33)	(6)
Smoker-group/age									
smokers-70-	27 (100)	245	(11)	(41)	(7)	(11)	(22)	(4)	(4)
smokers-60-	14 (100)	385	(7)	(14)	(14)	(0)	(36)	(21)	(7)
smokers-50-	1 (100)	969	(0)	(0)	(0)	(0)	(0)	(100)	(0)
non-smokers-70-	15 (100)	733	(0)	(0)	(0)	(13)	(33)	(40)	(13)
non-smokers-60-	9 (100)	505	(0)	(22)	(11)	(22)	(0)	(33)	(11)
non-smokers-50-	3 (100)	273	(0)	(0)	(0)	(0)	(100)	(0)	(0)
Histology									
ADC	51 (100)	521	(4)	(10)	(8)	(8)	(35)	(25)	(10)
non-ADC	14 (100)	173	(7)	(64)	(7)	(7)	(7)	(7)	(0)
LC-NOS	4 (100)	119	(25)	(25)	(0)	(50)	(0)	(0)	(0)

*Data are the number of patients (percentage). VS: very short (TVDT <54 days), S: short (55-218 days), M: medium (219-400 days), L: long (401-1,499 days), eL: extremely long (≥1,500 days), with subdivisions of S1 (55 to 112 days). S2 (113-163 days) and S3 (164-218 days) (see the meaning of subdivision at the data analysis in the text).

2. Purpose

The purpose of lung cancer screening should be considered as "early detection of lung cancer" [8-11]. International recognition is here, but the recognition of Japanese stakeholders generally lags behind this. Decisions on various matters related to medical examinations should also be made based on the need to achieve this goal. In this post, I will discuss the surprising usefulness of LDCT screening and the ineffectiveness of CXR screening, which has traditionally been carried out by the government. Japan's lung cancer screening laws are decisions made by arbitrary and irresponsible people who are not based on medical data. In this text, I will state that a fact is a fact, and a medical-related mistake is a mistake. Those who ignore the invalidity of CXR, which I would like to emphasize in this article, are the leaders of lung cancer screening in Japan, and they are an extremely embarrassing position internationally. Representative organizations include those who recommend the use of CXR screening as a screening method and those recommended by the Lung Cancer Society. I guess they have never thought about the goal of detecting early lung cancer. In the main text, the author provides a tentative definition of early lung cancer and clarifies its content based on empirical experiments. If this is pursued correctly, the five-year survival rate after surgery for patients detected through screening should approach 100%. While exploring the findings described here, we conducted two [unadjusted] LDCT screening demonstration experiments in Nagano Prefecture, and in both cases, the five-birth rate reached over 90%. This is a fact. Tumor volume doubling times according to age and smoking history of examinees have also been calculated and published [1-5].

3. Person in Charge of Demonstration Experiment (First Experiment)

Main researcher is Shusuke Sone, we believe that this recommendation is the cause of poor treatment results for lung cancer in Japan.

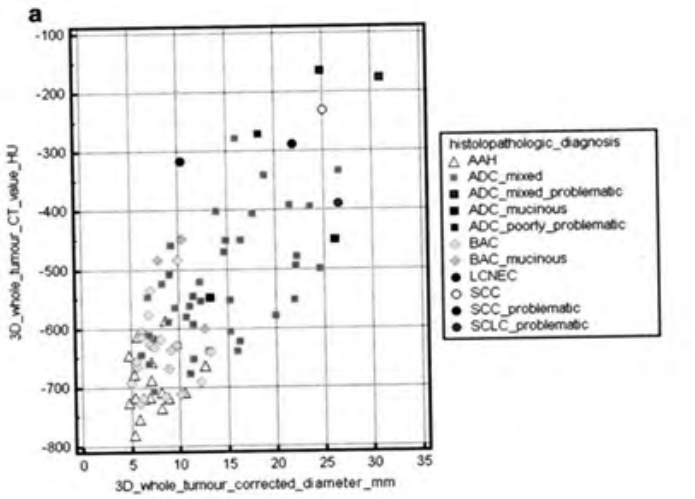
4. Temporary Definition of Early Lung Cancer

The tentative definition for this demonstration experiment is "Lung cancer that has no regional lymph node metastasis at the time of surgery, no local recurrence during 5 years of post-surgery

follow-up, and has not caused distant metastasis." (In the demonstration experiment, CT images of test takers who passed this provisional definition were examined. None of the test takers passed conventional CXR screening).

5. Size of Lung Cancer and CT Value Detected by LDCT Screening (Plot)

Based on my clinical experience, the author has judged that it is possible to detect masses larger than 3 mm in size with LDCT screening. In order to detect the early-stage lung cancer tentatively defined here, we can use this figure to determine how small a lesion must be discovered [L] and the heaviest mass], the above provisional early-stage lung cancer was determined (Figure 1). Write the name of histopathological diagnosis in the right margin. The "empty triangle" distributed at the lower left of the figure was a n AAH lesion (atypical adenomatous hyperplasia), pale and small, 4-12 mm in size, and the CT value was lower than -600 HU. The boundary between small, low-density lung cancer and AAH was not clear. In the upper right side of the figure, you can see five foci of "problematic". These did not correspond to the tentative definition of early lung cancer (all others were early lung cancer). The size of the foci that were not early lung cancer was 1 It is a highly concentrated lesion with a size of 0-31mm and a CT value of -310~-400HU or more. Parenchymal tumors larger than 10mm in size are generally rapidly progressing masses other than adenocarcinoma; The TVDT of the above tumors was short, progressed rapidly, and was often problematic.



Figure

6. CT Findings of Early Lung Cancer Detected by CT Screening

1) The entire mass has ground-glass opacity (GGO), the average CT value is paler than - [minus] 200 HU [e.g. - minus 300 HU], and its diameter is 14 If the size is less than a millimeter, it is considered early lung cancer.

2) Mixed ground-glass density [for lung cancers where the periphery of the tumor has a ground-glass density and the center has a dense zone (central dense zone, CDZ), if the diameter of the CDZ is 14 mm or less, it is considered early lung cancer].

3) If the entire mass is thick and denser than -150 HU [parenchymal, soft tissue density mass], and the maximum diameter is less than 10 mm, it is probably suspected of early lung cancer.

7. Testing Method Suitable for Lung Cancer Screening

Facts confirmed through demonstration experiments have been published in American and European journals, and based on these, screening experts believe that the LDCT method is a necessary and sufficient testing method for early detection of lung cancer. I will inform the person. Like the experts in the United States and Europe, I am convinced that the outdated and outdated CXR method is incapable of achieving the benefit of test subjects, that is, the early detection of lung cancer. Furthermore, although there are many cases of lung cancer in non-smokers in Japan, these are mainly adenocarcinomas, so the tumors shown in the figure are the main lesions. Therefore, in order to visualize this, it was found that it is important to have high sensitivity to "mass shadows mainly composed of ground glass density." CXR screening is inadequate in its ability to visualize these conditions, resulting in a low detection rate. Therefore, CXR is inappropriate for screening non-smokers, and we completely disagree with the Lung Cancer Society's guidelines that recommend CXR. L 5-year postoperative survival rate of lung cancer patients detected by DCT screening; In the L DCT examination, the rates were 92% (initial experiment at Shindai) and 94% (annual experiment at Azumi Hospital, calculations by Dr. Hanaoka). In contrast, the famous report by Dr. Sobue et al. using the conventional CXR method showed that the difference was 15%, and I hope that those involved in medical examinations fully understand this large disparity [1]. In a recent case-control study [CXR screening promoters conducted in Miyagi, Gunma, Niigata, and Okayama], the survival rate was reported to be 48-61% [however, these results are not based on CXR alone, but rather on sputum cells]. This is the result of combined diagnosis [2].

8. Overdiagnosis by LDCT

It has been said that many lung cancers detected by LDCT will not be the cause of death. However, according to the authors' inference [3-5], the overdiagnosis that they imagined was only 13% of the lung cancers detected by LDCT. Subsequently, quantitative measurements using the developed semi-automatic tumor size measurement software may further reduce the number of tumors.

9. Discussion

The quantitative nature of L DCT scans has the potential for further development. Allows calculation of tumor volume doubling time. In the Netherlands, the third international center for LDCT screening, a screening called the NELSON study is being conducted, in which short-term follow-up observations are conducted on people who test positive for lung cancer to determine who needs final detailed testing. The author's demonstration experiment in

Nagano [this is the author's first base, and the activity led by Professor Henschke of Cornell University in New York, which was launched around the same time and also collects international data, was also the first international announcement. [Although it was one year later than Nagano, it can be called the second base]. The tumor volume doubling time, TVDT, of Nagano test subjects has been investigated and has already been announced (Lung cancer screening test subjects' information by age group, sex, histopathological diagnosis, and smoking history).

10. Summary

We reported the results of using low-dose CT scans for lung cancer screening. 1. Lung cancer screening should be performed using the L DCT method. 2. The CXR method should not be used because the images for detecting lesions are inferior. 3. A tentative definition of early-stage lung cancer is made, and many early-stage lung cancers are detected by using LDCT. 4. CT images of early-stage lung cancer were clarified. 5. The 5-year postoperative survival rate for lung cancer detected by LDCT has reached over 90%. LDCT screening easily detects many early lung cancers. There is a concern that these may be overdiagnosis, but according to the authors' study, the number of suspected cases of overdiagnosis is only 1.3 %, and if the semi-automatic measurement method of CT images that has been developed since then is used in conjunction with this, it is expected that these cases will decrease even further. is expected.

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