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RADIATION RISK OF LUNG CANCER INCIDENCE WITH REGARD TO HISTOLOGICAL TUMOR TYPE

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1. Introduction

These are the results of the first analysis of lung malignant neoplasms incidence for different histological types in male Mayak Production Association workers with follow up longer than 50 years. The risks of cancer incidence are derived for the first time using the recently updated organ-specific dose estimates, Mayak doses-2008 (MWDS 2008).

2. Objectives

The estimation of radiation risk for lung cancer at prolonged occupational exposure for different histological types of tumor.

3. Study Population and Methods

The cohort included 16,685 male workers employed at the reactors, radiochemical and plutonium production facilities during 1948-1982 (Table 1). This cohort was followed up to the first cancer diagnosis ignoring non-melanoma skin cancers (NMSC), non-cancer death, migration from Ozyorsk or 31 December 2004, which ever was the earlier. This represents 389,154 person years of experience. 1,753 workers had cancer and 414 had lung cancer. Histological verification was available for 77.5% cases (Fig.1). Information on external gamma doses was available for all 100% of workers, but only 4,715 (37.7%) individuals of potentially exposed to internal radiation were examined for 239Pu body burden. Average accumulated external dose to lung was 0.48 gray (Gy), average accumulated Pu dose – 0.11 Gy. Workers from the reactors, non-exposed to plutonium, without bioassay measurements, were regarded as the monitored subjects with zero accumulated dose for the purposes of risk analyses. For workers from the radiochemical and plutonium production facilities, who were not subject to bioassay measurements, a categorical based surrogate variable using methods described elsewhere (1) was introduced to account for effects of internal alpha-radiation for the risk assessment.

Model parameters of the MN incidence rate were estimated with the Epicure software (2). The rate model has the form $\lambda=\lambda_0 \times [1+ERR]$. Background ($\lambda_0$) was adjusted for attained age, smoking status and calendar year. The ERR function were expressed as the sum of excess risks associated with external exposure (10 lagged external lung dose), monitored plutonium exposure (10-year lagged plutonium lung dose) and unmonitored plutonium exposure (high and low plutonium surrogates) as follows: **ERR= ERRext +ERRpumon +ERRpuunmon,** where ERRext, ERRpumon and ERRpuunmon represents the excess risk associated with external exposure, monitored plutonium exposure and unmonitored plutonium exposure respectively.

Table 1: Characteristics of the study cohort

Characteristics	Reactor plant		Radiochemical plant		Plutonium plant			
	N	%	N	%	N	%	N	%
Number of workers	4,194	25.1	6,859	41.1	5,632	33.8	16,685	100.0
with known vital status	4,000	95.4	6,469	94.3	5,389	95.7	15,858	95.0
provided with external gamma radiation data	4,194	100.0	6,859	100.0	5,632	100.0	16,685	100.0
examined for Pu body burden	209	5.0	2,532	36.9	1,974	35.0	4715	37.7*
Average accumulated dose from external gamma radiation to lung, Gy	0.47		0.71		0.20		0.48	
Average accumulated dose from internal alpha -radiation to lung from Pu^{239}, Gy	0.03		0.07		0.18		0.11	

*-among 12,491 workers of radiochemical and plutonium plants who have potential Pu exposure

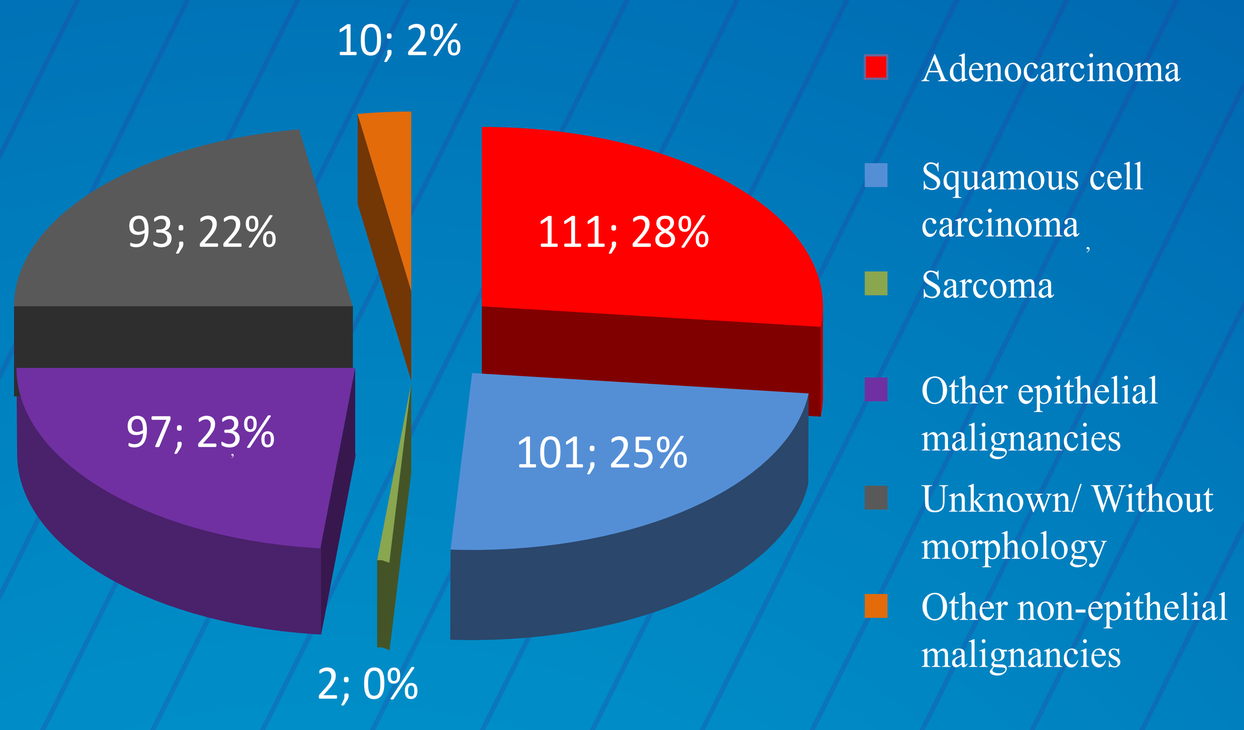

Fig.1 Histology group definitions based on Table 43 of solid cancer incidence in Atomic Bomb Survivors 1958-1998 (2007) Preston et al. Radiation Research 168, 1-64

4. Results

Risk estimates for lung cancer in general and for histological types of lung cancer from external dose, internal plutonium lung dose and the high plutonium surrogate are shown in Table 2. A steeper dose-response relationship was found for adenocarcinoma lung cancer compare to other lung cancer types for plutonium internal dose to the lung, external dose and also for combined plutonium surrogate categories 5&6, which includes workers employed at the main workshops of plutonium production facility during 1948-1953. The ERR/Gy for adenocarcinoma lung cancer in relation to internal plutonium dose was 30.4 (95% CI: 15.4; 66.6), which was about 10-fold higher than for squamous-cell lung cancer (ERR/Gy= 2.95; 95% CI: 0.32; 7.84) and 5-fold higher than for other epithelial neoplasms (ERR/Gy=5.77; 95% CI: 1.78; 14.05). For external dose, the ERR/Gy for adenocarcinoma was 1.08 (95% CI: 0.23; 3.38), which was 14 times larger than the estimate for squamous-cell lung cancer (ERR/Gy= 0.08; 95% CI: <0- 0.56) and about twice that for other confirmed epithelial lung cancers (ERR/Gy= 0.50; 95%CI: 0.01-1.54). For workers who were potentially exposed to plutonium, but not monitored, only significant association was observed for adenocarcinoma (ERR/Gy=3.26; 95% CI of 0.16; 11.20) for combined surrogate category 5&6.

Table 2: The excess relative risk per Gy (ERR/Gy) of lung cancer at different histological types of tumor for males with 95% CI, no modifying factors taken into account

Parameter	Adenocarcinoma	Squamous	Other epithelial	Unknown /Without morphology	Lung MNs
External lung dose	1.08 (0.23; 3.38)	0.08 (<0; 0.56)	0.50 (0.01, 1.54)	-0.14 (-0.18; -0.10)	0.24 (0.04; 0.53)
Plutonium lung dose	30.42 (15.43; 66.59)	2.95 (0.32; 7.84)	5.77 (1.78; 14.05)	1.79 (1.21; 2.46)	7.64 (5.09; 11.13).
Plutonium Surrogate Category 5-6	3.26 (0.16; 11.20)	0.11 (-0.84, 2.24)	1.24 (-0.63; 5.60)	-0.01 (-0.14; 0.15)	0.98 (0.03; 2.42)

5. Discussion

In the current dosimetry system (MWDS 2008) internal doses from alpha-radiation are averaged over the whole lung without accounting for non-uniformity of the radionuclide microdistribution in lung tissue. There were a lot of studies on the dynamics of plutonium microdistribution in lung after intake of inhaled nuclide. These studies demonstrated a highly non-uniform distribution in lung, while most of the radionuclide was retained in the upper pulmonary lobes and peripheral regions, which could be explained not by its high intake in these compartments, but rather by its slower clearance due to the worst blood and lymph circulation. Therefore, absorbed dose to peripheral regions of bronchioles and alveolar-interstitial compartment might be higher than that averaged over the whole lung. Thus, when estimating risk not by homogenous dose, but rather by dose distribution, ERR might be significantly lower for adenocarcinoma localized at the periphery.

The squamous-cell cancer was mainly localized in central lung compartments, which were exposed to higher doses in the process of plutonium intake and in the early period after exposure termination. Thus, estimated ERR for squamous-cell cancer, obtained in the present study may be underestimated. In addition, the lung tissue contained the target-cells located at the certain depth such as basal and secretory cells in the BB region, secretory cells in the bb region, Clara cells and Type II pneumocytes in the alveolar-interstitial compartment (AI). It is well-known that not only the diameter of airways, but also the thickness of epithelial cover decreased from 55 to 15 μm, on average, with a larger distance from the center to periphery. At the same time, the accessibility of target-cells for alpha-particles from plutonium also enhanced.

6. Conclusions

The study proved importance of epidemiological analysis of radiation risk based on incidence data, considering histological tumor type in particular. Besides the present study emphasizes significance of further studies in the course of internal dosimetry improvement in the field of Pu microdistribution in lung tissue, as well as more thorough study of non-radiation factors effect.

References

1. Shilnikova, N.S., et al., Cancer mortality risk among workers at the Mayak nuclear complex. Radiat Res, 2003. 159: p. 787-98.
2. Preston D. Epicure User's Guide. – USA, 1993. – 330 p.

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