Risk of chronic obstructive pulmonary disease in a cohort of workers occupationally exposed to ionizing radiation over prolonged periods

Tamara Azizova¹, Galina Zhuntova¹, Evgenia Grigorieva¹, Maria Moseeva¹, Maria Bannikova¹, and Evgeniy Bragin¹

¹Southern Ural Biophysics Institute, Ozyorsk, Russia

Introduction
Mayak Production Association is a Russian large-scale nuclear enterprise producing weapon-grade plutonium which was set in operation in 1948. Equipment defects and irregularity of technology process, low level of production mechanization and automatization in early years of the enterprise operation caused high levels of alpha-radioactivity in occupational air [1]. As Mayak PA workers did not use individual protection means for organs of respiratory system, alpha-particles of plutonium deposited in workers’ organisms via inhalation and were accumulated in main organs of plutonium deposition (lung, liver, bones) [2]. The first plutonium-induced pulmonary fibrosis (an early tissue reaction) was diagnosed in a plutonium production plant worker in 1956 [3].

The present study was aimed to assess the risk of chronic obstructive pulmonary disease (COPD) in workers of the Mayak PA exposed to internally deposited alpha-particles.

Material and methods
The study cohort included Mayak PA workers first employed at one of the main facilities (industrial reactors, radiochemical and plutonium production plants) in 1948–1982, in total 22,377 individuals (with 25% of females).

The follow-up of the cohort started with a date when a worker was hired and lasted until the earliest of the following events: date of COPD diagnosis, date of death, 31.12.2008, date of the last available medical record for migrants and residents with unknown vital status.

By the end of the follow-up vital status data was available for 95.0% of cohort members of whom 53.5% had deceased and 46.5% were alive. Information on disease incidence through the entire follow-up period was collected for 95.0% of workers, data on smoking status was available for 97.0% of workers with quantitative parameters estimated for 51.0% of ever-smoking workers.

To perform analyses, estimates of absorbed external and internal radiation doses were provided by dosimetry system MWDS–2008 [4].

Relative risk (RR) and excess relative risk per unit dose (ERR/Gy) were calculated based on maximum likelihood using AMFIT module of EPICURE software [5]. Differences were considered as statistically significant with p<0.05.

Results
The analysis demonstrated that COPD incidence in the Mayak PA worker cohort was significantly associated with sex, attained age, facility type, smoking status and index, calendar period and hazardous production factors which workers had been exposed to before employment at the Mayak PA (coal dust, chemicals, etc.).

The categorical analysis showed an increase of COPD risk estimates with increasing radiation doses, but significant ERR=1.30 95% CI: 1.04, 1.62) was revealed only in workers exposed to internally deposited alpha-particles at lung absorbed doses exceeding 0.1 Gy.

The table below summarizes results of ERR/Gy analysis for COPD incidence following external and internal radiation exposure.

No significant association of COPD incidence was observed with dose from external gamma-rays. The risk gained significance only after exclusion of adjustments for smoking and dose from internal alpha-radiation exposure.

To improve the accuracy of estimates of radiogenic risks for the study cohort, further studies are required to take into account characteristics of alpha-active aerosols used at the plutonium production and radiochemical plants in addition to occupational radiation exposure doses as well as to investigate a combined effect of occupational radiation exposure and smoking.

Conclusion
The study provides evidence to increased risk of COPD in the cohort of workers occupationally exposed to internal alpha-radiation.
Table COPD incidence risk in relation to external gamma-ray and internal alpha-particle exposures (ERR/Gy)

| Follow-up periods (0 year lag) | ERR/Gy (95% CI) | Внешнее γ-облучение | Внутреннее α-облучение |
|-------------------------------|-----------------|----------------------|------------------------|
| over the whole dose range     |                 |                      |                        |
| 1948–2008                     | 0.03 (-0.05; 0.14) | 0.79 (0.17; 1.78)    |
| 1948–1960                     | -0.06 (-0.15; 0.08) | 0.15 (na; 1.45)     |
| 1961–2008                     | 0.10 (-0.02; 0.26)  | 1.19 (0.32; 2.53)    |
| 1961–2008 follow-up period    |                 |                      |                        |
| Analyses with imposed lags    |                 |                      |                        |
| 5 years                       | 0.09 (-0.03; 0.25)  | 1.14 (0.22; 2.61)    |
| 10 years                      | 0.08 (-0.04; 0.23)  | 1.13 (0.15; 2.75)    |
| 15 years                      | 0.09 (-0.04; 0.25)  | 1.28 (0.19; 3.08)    |
| 20 years                      | 0.11 (-0.03; 0.29)  | 1.94 (0.39; 4.50)    |
| Analysis without adjustments for risk factors |       |                      |                        |
| Smoking                       | 0.16 (0.04; 0.32)  | 0.79 (0.19; 1.69)    |
| Alpha-radiation               | 0.20 (0.08; 0.34)  | 0.40 (0.04; 0.93)    |
| Alpha-radiation and smoking   | 0.24 (0.12; 0.40)  | 0.39 (0.04; 0.88)    |
| Alpha-radiation, smoking and facility type | 0.12 (0.03; 0.22) | 0.45 (0.10; 0.94)    |
| Analysis restricted with data on workers of |       |                      |                        |
| Facility type:                |                 |                      |                        |
| Reactors                      | 0.12 (-0.11; 0.50) | –                    |
| Radiochemical plant           | -0.09 (-0.26; 0.18) | 0.63 (na; 2.46)     |
| Plutonium production plant     | 0.19 (0.004; 0.48) | 1.65 (0.38; 3.97)    |
| | $p_1$ = 0.09 | $p_1$ = 0.36 |
| Sex:                          |                 |                      |                        |
| Males                         | 0.10 (-0.03; 0.27) | 1.45 (0.32; 3.20)    |
| Females                       | 0.13 (na; 0.67)  | 0.74 (na; 3.10)     |
| | $p_2 > 0.50$ | $p_2 > 0.50$ |
| Attained age (years):         |                 |                      |                        |
| < 40                          | 0.32 (na; 1.24)  | 0.37 (na; na)       |
| 40 – 49                       | -0.03 (na; 0.27)  | 0.88 (na; 5.91)     |
| 50 – 59                       | -0.02 (-0.17; 0.23) | 1.47 (na; 4.15)    |
| 60 +                          | 0.32 (0.03; 0.82) | 0.82 (na; 3.85)     |
| | $p_3$ = 0.12 | $p_3$ = 0.36 |
| | $p_4$ = 0.24 | $p_4$ = 0.37 |
| Smoking status:               |                 |                      |                        |
| Never-smokers                 | 0.10 (na; 0.57)  | 0.87 (na; 2.96)     |
| Former smokers                | 0.40 (0.00; 1.28) | 2.09 (na; 9.59)     |
| Smokers                       | 0.10 (-0.05; 0.33) | 1.30 (na; 3.70)    |
| | $p_5 > 0.50$ | $p_5 > 0.50$ |
| Smoking index (pack-years):   |                 |                      |                        |
| 0 (did not smoke)             | 0.10 (na; 0.57)  | 0.87 (na; 2.96)     |
| <10                           | -0.15 (na; na)   | 0.94 (na; na)       |
| ≥ 10                          | 0.15 (-0.01; 0.37) | 1.56 (0.25; 3.64) |
| | $p_6$ = 0.37 | $p_6 > 0.50$ |
| Pre-employment hazardous factors: |           |                      |                        |
| Yes                           | 0.15 (-0.02; 0.40) | 0.52 (na; 2.09)     |
| Potentially                   | 0.02 (-0.17; 0.37) | -0.05 (na; na)     |
| No                            | 0.12 (-0.12; 0.53) | 4.08 (1.44; 8.54) |
| | $p_7 > 0.50$ | $p_7 = 0.01$ |

na –95% CI were not defined

$p_1$ – test for heterogeneity between workers of radiochemical and plutonium production plants;

$p_2$ – test for heterogeneity between male and female workers;

$p_3$ – test for heterogeneity among various age groups of workers;

$p_4$ – test for log-linear trend for ERR/Gy with attained age;

$p_5$ – test for heterogeneity among groups of workers with various smoking statuses;

$p_6$ – test for heterogeneity among groups of workers with various smoking indexes (< 10 и ≥ 10 pack-years);

$p_7$ – test for heterogeneity between groups of workers exposed and unexposed to hazardous industrial factors prior to Mayak PA employment.
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