

# **Associations Between Potential Risk Factors and Malignant Liver Cancer Among Mayak Plutonium Facility Workers**

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# Purpose of Study

- To examine the relative contribution of specific risk factors to **liver cancer** occurrence in Mayak workers
- To compare liver cancer spectra after **Pu-239** and **Th-232** exposures of humans

# Case-Control Study Design

Study design developed by:

- Dr. Zoya B. Tokarskay, **SUBI**
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***SUBI: Southern Ural Biophysics Institute***

# Types of Liver Cancer Evaluated

- Hemangiosarcoma (**HAS**)
- Hepatocellular cancer (**HCC**)
- Cholangiocarcinoma (**CHC**)

# Morphologically Confirmed Tumors

1972-1999

- Hemangiosarcoma (**HAS**) – 11
- Hepatocellular cancer (**HCC**) – 27
- Cholangiocarcinoma (**CHC**) – 6

# Matching Criteria

- Gender
- Year of birth
- Year started work
- Workplace and type of work
- Case-control ratio – 1:2 or 1:4

*N = 111*

# Gamma-Ray Dosimetry

- **Mayak Dosimetry Monitoring Service** registered gamma-ray exposures
- **Individual film badges** used for gamma-ray exposure monitoring
- **Daily monitoring** initially (1948)
- **Weekly** and then **monthly** monitoring later followed
- **Errors** initially 60%; later 30%

# Pu-239 Dosimetry

- **SUBI Laboratory of Internal Dosimetry** estimated Pu-239 body burdens
- **Urine bioassay** used along with Pu biokinetic model
- **Double phosphate precipitation** method used to estimate Pu-239 in urine
- **Minimum detectable Pu-239** in urine was 4 mBq (corresponds to 0.26 kBq body burden)

# Time-Dependent Dosimetric Quantities

- The **Pu-239 body burden** and **alpha radiation doses** estimated using SUBI biokinetic model
- Evaluations conducted for **specific times** of interest
- Associated **uncertainties not available**

# Quantifying Smoking and Alcohol Consumption

- Smoking index (**SI**):
  - Number of cigarettes per day times years smoking
- Alcohol consumption:
  - Rare drinker, moderate drinker, heavy drinker

# SAS-Based Statistical Methods

- Means compared using **t test**
- Odds ratios (OR) significance based on  $\chi^2$
- **Nonparametric:** Man-Whitney, Kolmogorov-Smirnov
- **Multivariate:** multiple logistic regression
- **Cox regression** for continuous variate analyses

# Results

- HAS (OR=18.5) and HCC (OR=6.4) were significantly ( $p < 0.05$ ) associated with alpha irradiation
- HCC was more strongly associated with alcohol consumption than with radiation
- CHC was not associated with low dose radiation ( $p > 0.05$ )

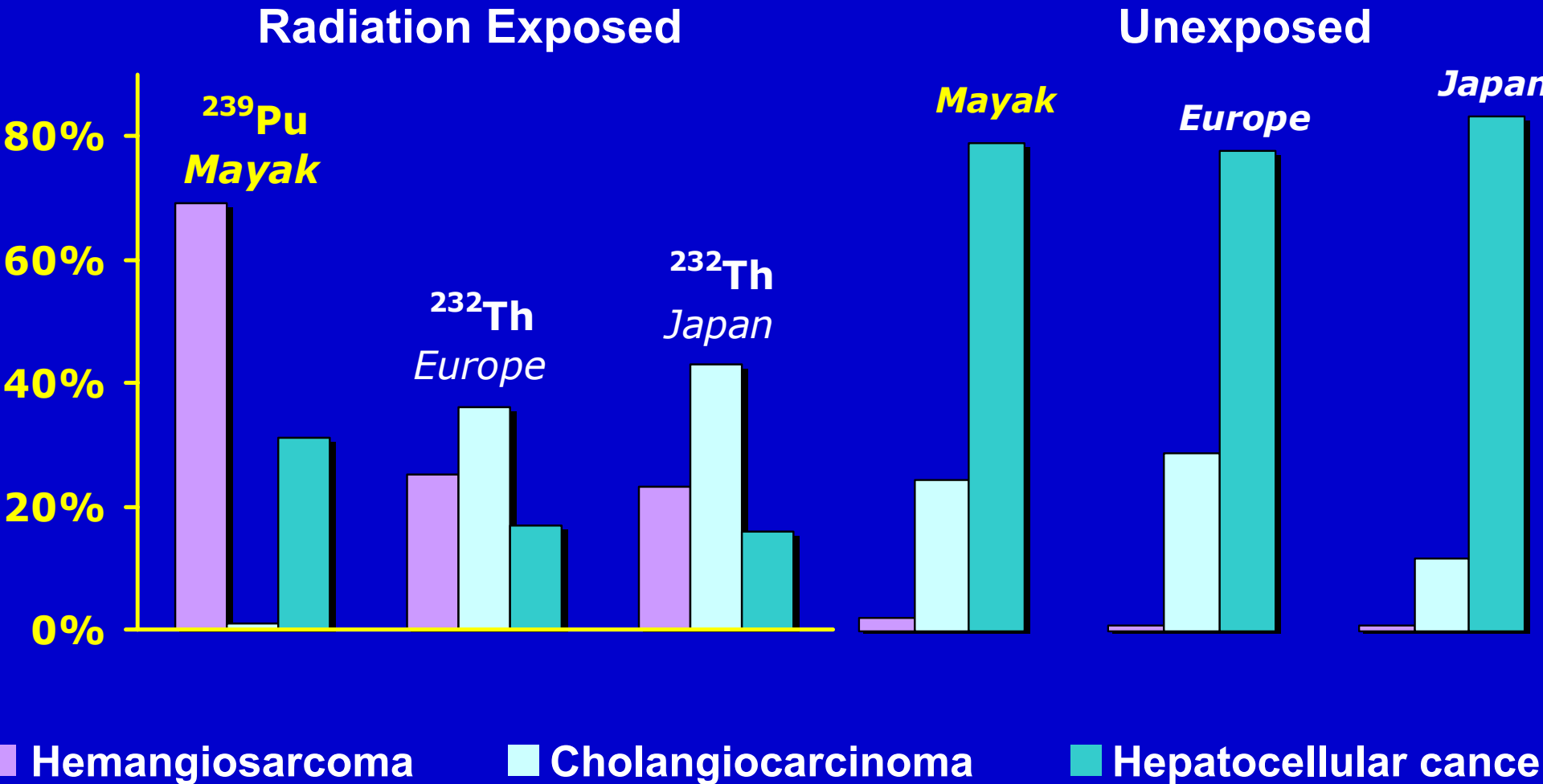
# Results (continued)

- Low dose, low dose rate gamma irradiation was not associated with liver cancer occurrence ( $p>0.05$ )
- Results are consistent with a threshold for gamma-ray-induced liver cancer
- Smoking was not found to influence liver cancer occurrence ( $p>0.05$ )

# Comparison of $^{239}\text{Pu}$ and $^{232}\text{Th}$ -induced Liver Tumors

|                     | $^{239}\text{Pu}$                                   | Thorotrast  |
|---------------------|---|---|
| Type of study       | case-control  | cohort  |
| Radionuclide intake | inhalation  | intravascular                                     |
| Types of compounds  | soluble and other                                   | insoluble   |
| Microdistribution   | hepatocytes,<br>Kupffer cells,<br>endothelial cells | Kupffer cells,<br>endothelial cells,<br>sinusoids |
| Exposure period, yr | 22 – 43   | 20 – 50   |

# Liver Tumor Spectra for Different Populations



# Conclusions

- **HAS and HCC are both associated with alpha irradiation**
- **Alcohol was more strongly associated with HCC than alpha radiation**
- **The liver tumor spectra differs for Pu-239 and Th-232 induced cancers**
- **Results obtained do not support the general validity of the LNT model**

# Statistical References

- **Breslow and Day 1980**
- **Fleiss 1981**
- **Rothman 1996**
- **SAS 8.02 1999–2001**