

INTRODUCTION

- Residential radon exposure is a significant risk factor for lung cancer, being the second cause after tobacco consumption, and the first in never smokers.
- According to the World Health Organization (WHO), radon is responsible for approximately 3% to 14% of all lung cancer cases.
- Despite this, the molecular mechanisms underlying radon-induced carcinogenesis remain poorly understood.
- In this study, we investigate the relationship between residential radon exposure and a set of molecular alterations in non-small cell lung cancer (NSCLC) patients.

METHODS

- A total of 207 patients with confirmed NSCLC were included in the study.
- Radon exposure was measured at an Accredited Laboratory using alpha-track radon detectors (CR-39; Radosys Ltd, Budapest, Hungary) which are the most reliable technique and recommended by the Nuclear Safety Council.
- Pre-treatment tumor biopsies were analyzed using next-generation sequencing (NGS).

RESULTS

- A total of 207 patients with confirmed NSCLC were included in the study. Patient characteristics are described in Table 1.
- At diagnosis, 65% had metastatic disease, 23% were at a locally advanced stage (stage IIIA-C), and 12% were diagnosed at an early stage (stage IA–IIB).
- The median residential radon concentration in our cohort was 78 Bq/m³ (IQ25-75%: 45-137); min 4 Bq/m³, max 1,035 Bq/m³.
- A molecular alteration was identified in 141 patients (68%). Specifically, 6% of tumors had an ALK translocation, and 10% had EGFR common mutations. Other targetable alterations included KRAS G12C mutations (10%), BRAF V600E (2%), MET amplification (1%), MET exon 14 skipping mutations (2%), and HER2 alterations (including amplification or exon 20 insertions) in 2% of cases. Additionally, ROS1 fusions and RET fusions were each identified in 0.6% of tumors.
- Patients with targetable molecular alterations (excluding BRAF V600E and KRAS G12C mutations) had higher levels of residential radon (139 Bq/m³ vs. 68 Bq/m³; p < 0.001). Those with druggable gene fusions had even higher levels (144 vs. 88 Bq; p < 0.001).

Characteristics	N=207 (%)
Sex	
• Male	126 (60.87)
• Female	81 (39.13)
Histology	
• Adenocarcinoma	147 (71.01)
• Squamous	38 (18.36)
• Others	22 (10.63)
Age at diagnosis (median, Min-Max)	65 (30-91)
Smoking habit	
• Smoker	77 (37.30)
• Former smoker	112 (53.98)
• Never smoker	18 (8.72)
PD-L1	
• Yes	170 (82.13)
• Not available	37 (17.87)

Table 1. Patient characteristics

- ALK-positive NSCLC patients had higher radon exposure than ALK-negative cases (142 Bq/m³ vs. 74 Bq/m³; p=0.006).**
- Tumors with a BRAF mutation (including non V600E) had lower exposure (39 Bq/m³ vs. 78 Bq/m³; p=0.034).**

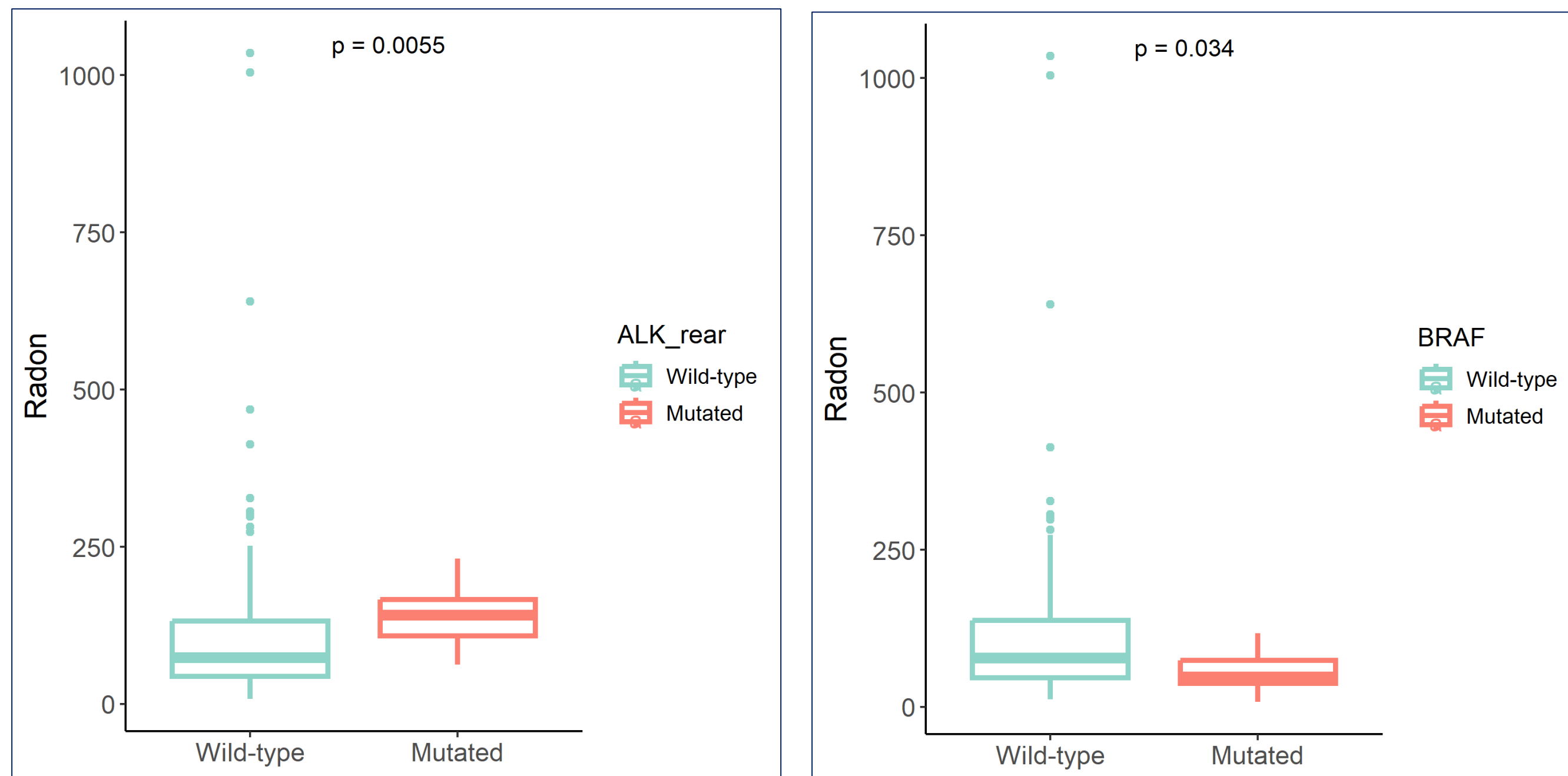


Figure 1. Association: residential radon concentration and molecular alterations

DISCUSSION AND CONCLUSION

- Druggable gene fusions in non-small cell lung cancer are significantly associated with higher levels of residential radon exposure.**
- These findings suggest a potential link between residential radon exposure and the development of specific molecular alterations, particularly ALK rearrangements.**
- Further research is warranted to explore the biological mechanisms underlying this association and to assess the implications for lung cancer prevention and targeted therapy strategies.**

REFERENCES & ACKNOWLEDGEMENTS

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- Galician Radon Laboratory, a Spanish laboratory accredited by the Spanish National Entity of Accreditation (Entidad Nacional de Acreditación – ENAC)
IDIPHISA - Oncology Laboratory - Liquid Biopsy
Spanish Lung Cancer Group (SLCG)