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# Radiological and chemical exposures and risks of cancer in the Constances cohort (COREXCA)

Olivier Laurent<sup>1</sup>, Philippe Renaud<sup>1</sup>, David Broggio<sup>1</sup>, Eric Blanchardon<sup>1</sup>, Serge Dreuil<sup>1</sup>, Claire Gréau<sup>1</sup>, Caroline Vignaud<sup>1</sup>, Sophie Ancelet<sup>1</sup>, Olivier Armant<sup>1</sup>, Marie-Odile Bernier<sup>1</sup>, Enora Cléro<sup>1</sup>, Christelle Durand<sup>1</sup>, Teni Ebrahimian Chiusa<sup>1</sup>, Anais Foucault<sup>1</sup>, Marcel Goldberg<sup>2</sup>, Sabine Guérin<sup>3</sup>, Christelle Huet<sup>1</sup>, Emeline Lequy<sup>2</sup>, Jean-Michel Métivier<sup>1</sup>, Stéphane Grison<sup>1</sup>, Chrystelle Ibanez<sup>1</sup>, Géraldine Ielsch<sup>1</sup>, Dmitry Klokov<sup>1</sup>, Virginie Monceau<sup>1</sup>, Hervé Roy<sup>1</sup>, Chantal Guihenneuc<sup>4</sup>, Klervi Leuraud<sup>1</sup>, Nathalie Velly<sup>3</sup>, Marie Zins<sup>2</sup>.

Affiliations: 1. Institut de Radioprotection et de Sûreté Nucléaire (IRSN), Fontenay-aux-Roses/Cadarache, France. 2. UMS 011 Inserm/UVSQ/Uparis Cité/UP Saclay "Cohortes épidémiologiques en population", Villejuif, France. 3. Ineris, ISAE, Verneuil-en-Halatte, France. 4. BioSTM — EA 7537, Université Paris Cité, France

## INTRODUCTION

### Background

Populations are exposed to ionizing radiation (IR) and chemical pollutants (CPs) at various levels, via multiple natural and artificial sources, in the context of the residential environment, workplace and/or for medical reasons (diagnostic or therapeutic procedures). The carcinogenic effects of IR are well documented above dose levels of 100 milliGrays, but still less well below. In addition, the effects of joint exposures to IR and CPs on cancer risks are poorly documented.

### Objectives

The first objective of COREXCA is to carry out the broadest possible reconstruction of life-long doses of IR and several carcinogenic CPs (cadmium, nickel and chromium) from environmental sources (e.g. : natural radioactivity, nuclear installations and other artificial sources) and occupational activities, but also medical exposures, received by around 80,000 participants of the French Constances cohort (<https://www.constances.fr/>).

The second objective will be to estimate cancer risks associated with the cumulative doses of IR and CPs received by these participants.



## MATERIALS AND METHODS

Reconstructions of environmental, occupational and medical exposures to IR will be performed by IRSN, through linkage of Constances data with several national databases on exposure to IR (e.g. the French national health data system SNDS involving medical exposures, retrospective radioactivity maps, SISERI system centralizing results of occupational exposures surveillance) and responses to a specific questionnaire.

Environmental exposures to CPs will be estimated by Ineris thanks to a linkage of Constances with the established PLAINE platform (Caudeville, 2015).

Occupational exposure to CPs will be estimated by UMS011 thanks to linkage of Constances with the CANJEM job-exposure matrix (Siemiatycki et al., 2018).

Statistical analyses (e.g., Cox models with time-dependent covariates) will be carried out by IRSN and will benefit from the expertise of biologists, supporting the exploration of specific hypotheses and interpretations. The use of innovative probabilistic models to deal with multiple correlated exposures such as Bayesian profile regression mixture models will be explored (Belloni et al., 2020). They allow simultaneously clustering individuals with similar risks and similar exposure characteristics and estimating the associated risk for each group.

Access to Constances data will be operated within a secure environment provided by CASD –Centre d'Accès Sécurisé aux Données (Ref. 10.34724/CASD)

## AVAILABLE DATA, ROADMAP AND PERSPECTIVES

The compilation of data needed to reconstruct several environmental exposures since birth (radon, fallout from worldwide nuclear tests and Tchernobyl accident) is in progress.

The linkage between residential histories and environmental data will be completed by the end of year 2022.



A specific questionnaire has been developed and will be sent to the 80,000 participants at the beginning of year 2023.

A PhD thesis starts in November 2022 to study the long-term effects of radon exposure during childhood (and beyond) as part of the RadoNorm project.

The measurement of radon concentrations will be conducted in the homes of 1000 Constances volunteers during winter 2023-2024 (also as part of RadoNorm)

Exposure estimates for occupational and medical exposures, as well as environmental exposure to CPs will be estimated by mid-2024.



Statistical analyses will be finalized by the end of year 2024.

Analysis results but also data created by COREXCA will become accessible to the scientific community, following the procedures of the Constances cohort charter (<https://www.constances.fr/charte.pdf>).

This will, in the long term, help to further improve the characterization of the carcinogenic effects of joint exposure to IR and other stressors, in support of radiation and chemical protection.

COREXCA is part of a broader long-term research program, which will include investigation of the effects of other multi-exposures (e.g., IR and environmental exposures to chemicals) and the study of risks and exposure biomarkers through the Constances biobank (Henny et al., 2020).

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**Contact:** olivier.laurent@irsn.fr