令和３年度原子力施設等防災対策等委託費

（低線量放射線による人体への影響に関する疫学的調査）事業

（原子力規制委員会原子力規制庁委託調査報告書）

令和４年３月

公益財団法人　放射線影響協会

本報告書は、原子力規制庁の委託業務として、（公財）放射線影響協会が実施した「令和３年度原子力施設等防災対策等委託費（低線量放射線による人体への影響に関する疫学的調査）事業」の成果を取り纏めたものです。

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Ⅰ．概　　要

令和 3 年度は、平成 27 年度に策定した健康影響評価計画に基づき、調査対象者の生死等情報の把握を行うとともに、令和元年度から利用が可能になったがん罹患情報を利用するため「がん登録等の推進に関する法律」に基づく手続きを行い、国立がん研究センターからリンケージデータを取得した。また、調査対象者に関する情報（被ばく線量、生死、死因等）の更新等を行った。なお、これらの個人情報の取得は、平成 27 年度から令和元年度までに実施した意思確認調査において、調査対象者の同意を得たうえで実施した。さらに、本事業の理解促進活動として、これまでに取得したデータをもとに解析した結果について学会発表、論文投稿等を行うとともに、ホームページ等により本疫学調査について情報発信した。

１．調査対象者に関する情報の更新等業務

１．１　調査対象者の被ばく線量に関する情報の更新

当協会放射線従事者中央登録センター（以下「中央登録センター」という。）から令和 2 年度までの被ばく線量情報等の提供を受け、放射線疫学調査ファイル（以下「疫学 DB」という。）に反映した。

１．２　調査対象者の生死等に関する情報の更新

本年度は、28,450 人の調査対象者について生死追跡調査を行い、1,352 市区町村に対し住民票の写し等の交付を請求し、全ての市区町村から計 28,450 人の調査対象者について住民票の写し等の交付を受け、その情報を疫学 DB に反映した。

１．３　調査対象者の死因情報の継続使用に関する手続き

統計法（平成 19 年法律第 53 号）第 33 条規定に基づき、人口動態調査死亡票の調査票情報の継続保有の申請を行い、厚生労働大臣から承認を受けた。

２．がん罹患情報の取得

本事業では、第Ⅵ期を開始した平成 27 年度から、放射線被ばくによる健康影響、特にがん発生に及ぼす影響を評価する際、その評価指標として死亡に加え、がん罹患も用いることとしている。令和 2 年度に厚生労働大臣から許諾された 2016～2017 年全国がん登録情報について、国立がん研究センターの全国がん登録データベースとのリンケージにより調査対象者のがん罹患情報を取得し、疫学 DB と合わせて利用するがん罹患情報のデータベース（以下「がん罹患情報 DB」という。）を更新し、がん罹患者の集計を行った。また、提供が開始された診断年 2016～2018 年全国がん登録情報について、同様に令和 3 年 5 月に利用申請を行い、令和 3 年 9 月に応諾されたため、がん罹患情報 DB を再度更新した。

３．委員会活動

本事業の的確かつ円滑な実行を目的として、個人情報の取扱い及び疫学研究に係る倫理的事項について審査を行う「倫理審査・個人情報保護委員会」並びに調査研究計画、調査の実

施方法及びがん罹患情報の活用方策について審査を行う「調査研究評価委員会」を設置した。また、「平成 28 年度放射線疫学調査あり方検討会」が策定した報告書を踏まえ、「放射線疫学調査あり方検討会フォローアップ委員会」を設置し、令和 4 年度以降の事業方針について審査を受けた。

４．本事業の理解促進活動

４．１　ホームページによる放射線疫学調査関連情報の周知

調査結果等について広く周知し、事業対象者の協力を得るために当協会ホームページ、放影協ニュース等による情報発信を行った。

４．２　国内外の論文投稿・学会発表

国内外の機関に積極的に引用される調査として専門家に認知されることを目的に、6 回の学会発表を行った。また、論文投稿を行い、4 編が公表された。

４．３　外部専門家との意見交換会

当協会主催の令和 3 年度 ICRP 調査・研究連絡委員会「外部専門家との意見交換会」に参加し、講演及び意見交換を行った。

Ⅱ．事業内容

１．調査対象者に関する情報の更新等業務

１．１　調査対象者の被ばく線量に関する情報の更新

第Ⅵ期調査（平成 27 年度～令和元年度）において設定した約 8 万人のコホートについて、中央登録センターから令和 2 年度までの被ばく線量情報等の提供を受け、疫学 DB に反映した。

１．２　調査対象者の生死等に関する情報の更新

調査対象者の死因情報及びがん罹患情報の取得等を確実に実施するために、調査対象者の住所地及び生死の情報を可能な限り最新の状態に保つ必要がある。調査対象者の住所地及び生死の確認（以下「生死追跡調査」という。）は、個人情報保護に留意しつつ、全国の市区町村（特別区及び政令市の行政区を含む。以下、同様。）から住民票の写し等を取得することにより行い、その結果の集計及び疫学 DB の更新を行った。

（１）生死追跡調査

平成 30 年度までは住民基本台帳法において消除された住民票（以下、除票と言う。）の保存期間は 5 年間と定められていたことから、1 人の調査対象者について少なくとも 4 年に 1 度の頻度で生死追跡調査を行ってきた。令和元年に同法が改正され、除票の保存期間が従来の 5 年間から 150 年間に延長されたが、がん罹患情報を取得するに当たり、調査対象者の最新の住所情報を必要とすることから、引き続き同じ頻度で生死追跡調査を行うこととしている。本年度は平成 27 年度から令和元年度に実施した意思確認調査において、本疫学調査の対象者となることに同意した 81,507 人のうち 28,450 人について生死追跡調査を行った。

以下に、本年度の生死追跡調査の結果を報告する。

１）住民票の写し等の交付請求及び取得

ｉ）住民票の写し等の交付請求

本年度は、(a)本年度中に当該調査対象者についての直近の生死追跡調査から 4 年が経過する者（平成 29 年度の生死追跡調査で住民票の写しを取得した者のうち、令和 2 年度に交付請求を行わなかった者）及び 3 年が経過する者（平成 30 年度に住民票の写しを取得した者）のうち一部の者、(b)前年度（令和 2 年度）の生死追跡調査において住民票の写し等の交付請求先の市区町村から他の市区町村への転出が判明した者並びに(c)前年度（令和 2 年度）の生死追跡調査において「該当者なし」等の理由で住民票の写し等を交付されなかった者のうち、再調査を行うこととした者、計 28,450 人の調査対象者について、1,352 市区町村に対し住民票の写し等の交付を請求した。

本年度、住民票の写し等を請求した調査対象者の内訳は**表１．１**の通りである。

ⅱ）住民票の写し等の取得

ⅰ）の住民票の写し等の交付請求により住民票の写し等を取得した者及び取得できなかった者は、その内容により以下の通りの区分に分類し、整理している。

① 住民票の写しを取得した者（氏名、住所等が変更されていないもの）
② 住民票の写しを取得した者（氏名、住所等が変更されているもの）
③ 除票の写しを取得した者（死亡による消除）
④ 除票の写しを取得した者（転出（海外への転出を含む。）による消除）
⑤ 住民票を確認できなかった者（「該当者なし」（調査対象者が当該の市区町村の住民ではなく、当該調査対象者の住民票が作成されていないことによる）のため）
⑥ 住民票を確認できなかった者（住民票の消除後 5 年（保存期限）以上経過のため）
⑦ 除票の写しを取得した者（不在住等の事由による市区町村長の職権による消除）
⑧ その他

本年度は、住民票の写し等の交付を請求した 1,352 市区町村の全ての市区町村から、計 28,450 人の調査対象者について、住民票の写し等の交付等による回答を得た。本年度に住民票の写し等の交付を請求した調査対象者のうち住民票の写し等を取得した者及び取得できなかった者の内訳は**表１．２**の通りである。区分①②④に該当する 27,725 人は生存を示す。【巻末参考資料 23 頁 表１．１参照】

表１.１　本年度に住民票の写し等の交付を請求した調査対象者の内訳

請求の内訳	人数
(a) 前回住民票の写しを取得した者[注-1]	27,155
(b) 前回転出除票の写しを取得した者[注-2]	1,293
(c) 前回「該当者なし」等の回答を得た者[注-3]	2
合計	28,450

注-1　直近の生死追跡調査から 4 年が経過する者（平成 29 年度の生死追跡調査において住民票の写しを取得した者のうち令和 2 年度に交付請求を行わなかった者）及び 3 年が経過する者（平成 30 年度に住民票の写しを取得した者）のうち一部の者の調査

注-2　前年度（令和 2 年度）の生死追跡調査において他の市区町村への転出が判明した者の調査

注-3　前年度（令和 2 年度）の生死追跡調査において、「該当者なし」等の回答を得た者のうち一部の者の再調査

表１.２　本年度に住民票の写し等を取得した者及び取得できなかった者の内訳

（令和 4 年 2 月現在）

区分		人数
住民票の写しを取得した者	①②	25,935
除票の写し（転出）を取得した者	④	1,790
内、国内の他市区町村への転出		1,772
内、海外への転出		18
除票の写し（死亡）を取得した者	③	717
該当者なし等の回答を得た者	⑤⑥⑦	8
その他（不交付）	⑧	0
合計		28,450

２）平成 27 年度以降の生死追跡調査の状況（累計）

第Ⅵ期調査（平成 27 年度～令和元年度）に実施した意思確認調査及び生死確認調査において、本疫学調査の調査対象者となることに同意した 81,507 人が第Ⅶ期調査（令和 2 年度～令和 6 年度）以降の生死追跡調査の対象となる。本年度の生死追跡調査の結果を反映し、平成 27 年度以降の調査対象者の生死追跡状況を集計した。

令和 4 年 2 月現在で次のとおりとなった。(1) 生存者は 78,730 人（男性 77,892 人、女性 838 人）、(2) 死亡者は 2,363 人（男性 2,358 人、女性 5 人）、(3)調査の結果追跡できなくなった者は 414 人（男性 408 人、女性 6 人）となった。

詳細は**表１．３**の通りである。【巻末参考資料 24 頁 表１． ２参照】

３）平成 3 年度以降の生死追跡調査の状況（年度推移）

全国の市区町村から住民票の写し等を取得することによる生死追跡調査を開始して 31 年が経過した。その間の生死追跡調査の状況（年度推移）を**図１．１**に示す。

４）生死追跡調査における「脱落」等の発生

ⅰ）追跡先住所不明

住民票の写し等の取得による生死追跡調査において、市区町村から「該当者なし」等の回答を受けた調査対象者の一部については、前年度までに取得した最新の住民票の写し等を当該市区町村に提示し、再度、住民票の写し等の交付請求を行った。他市区町村への転出が判明した者については、必要に応じて転出先の市区町村に対して追加の住民票の写し等の交付請求を行った。

しかしながら、調査対象者が転出元又は転出先の市区町村で転出又は転入の手続きをしないこと等により、調査対象者の転出先の住所が不明となることがあるため、「脱落」が発生することがある。

本年度は 8 人（本年度の調査対象人数の 0.03%に相当）の「脱落」があった。特に該当者が少ない累積被ばく線量 50mSv 以上の調査対象者（以下「50mSv 以上群」という。）の「脱落」はなかった。

ⅱ）海外転出

海外への転出が判明した調査対象者については、以降の追跡が困難であるため、生死追跡調査を継続しないこととしている。

本年度は 18 人（本年度の調査対象人数の 0.06%に相当）の海外転出があった。50mSv 以上群からの「海外転出」はなかった。

ⅲ）住民票の写し等の不交付

住民基本台帳法が平成 20 年 5 月に改正され、個人情報保護の観点から住民票の写しの交付請求に本人同意が必要となったことにより、以降、市区町村の判断によっては住民票の写し等が交付されない事例が生じた。住民票の写し等の請求先とな

った市区町村に対しては、本疫学調査の意義を説明すること等により、市区町村の理解及び協力を得ることに努めているが、やむを得ず住民票の写し等が交付されない場合は、意思確認調査において受領した当該の調査対象者の同意書を添付して交付請求を行うこととしている。本年度は 117 市区町村に住所を持つ調査対象者については、同意書を添えて住民票の写し等の交付請求を行った。

前述のとおり、不交付はなかった。

表 1.3　令和 2 年度以降の生死追跡状況（累計）

（令和 4 年 2 月現在）

追跡結果	人数（男　女）
(1) 生存	78,730（ 77,892　838）
(2) 死亡	2,363（ 2,358　5）
(3) 脱落	414（ 408　6）
（脱落の内訳）	
住所不明等[注-1]	414（ 408　6）
不交付[注-2]	0（ 0　0）
合計	81,507（ 80,658　849）

注-1　調査対象者本人から入手した住所情報に基づいて行う住民票の写し等の請求において、該当者なしの回答を得た、又は除票の保存期間経過、職権消除等の理由で、住民票の写し等を取得できずに脱落した調査対象者の数

注-2　市区町村の協力を得られなかったことにより、住民票の写し等を取得できなかった調査対象者の数

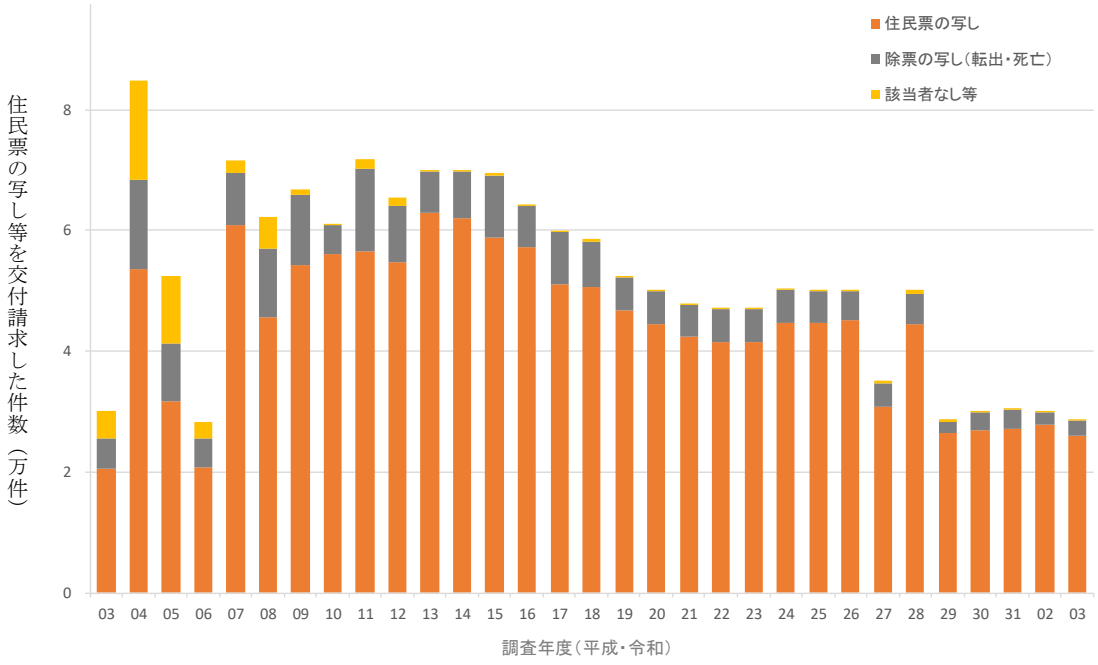


図 1.1　平成 3 年度以降の生死追跡調査の状況（年度推移）

（２）疫学 DB の管理等

本疫学調査の実施に当たっては、平成 11 年 3 月までに放射線業務従事者として登録した者のうち調査対象者となった 277,128 人についての情報を収めた疫学 DB を、インターネット及び当協会の計算機ネットワークから独立した計算機上に構築している。このデータベースの管理のために開発した「放射線疫学調査に係る情報処理システム」（以下「情報処理システム」という。）により、年度毎に行う生死追跡調査の対象者の抽出、市区町村長に提出するための住民票の写し等の請求書類の作成、交付を受けた住民票の写し等の記載事項等の計算機への入力並びに疫学 DB に登録された情報の更新及び修正を行ってきた。現在は、平成 27 年度から令和元年度にかけて実施した意思確認調査により本疫学調査の調査対象者となることに同意した約 8 万人の調査対象者について疫学 DB を更新することとしている。一方、意思確認調査により不同意の意思を表明した者については、疫学 DB の個人情報を匿名化した。

本年度は生死追跡調査において新たに入手した住民票の写し等の情報に基づき、疫学 DB を更新した。そのうち、転居（同じ市区町村での引越し）による住所の変更又は氏名の変更があった者は 1,613 人、転出による住所変更があった者は 1,790 人、死亡した者は 717 人、該当者なし等により追跡できなかった者は 8 人であった。

また、疫学 DB 及び情報処理システムについては、定期的に保守点検を行うことにより、その正常維持を図るとともに、データのバックアップを定期的に行い、データを適正に保管している。

１．３　調査対象者の死因情報の継続使用に関する手続き

統計法（平成 19 年法律第 53 号）第 33 条規定に基づき、令和 3 年 4 月 9 日に人口動態調査死亡票の調査票情報の継続使用の申請を厚生労働省に対して行い、同日に承認を受けた。

２．がん罹患情報の取得

平成 26 年度までの本疫学調査では、主に被ばく線量とがん死亡との関係を解析することで、低線量放射線の健康影響を評価してきたが、医療技術の進展等に伴いがんの致死率（致命率）が低下している現状を考慮し、健康指標として死亡だけでなく、がん罹患も調査することにより、より精度の高い健康影響の評価を行うことが必要となった。がん罹患情報に関しては、かつて一部の都道府県で地域がん登録制度があるのみであったが、平成 28 年 1 月に全国がん登録制度が発足し、居住地域に関わらず全国のがん罹患者の情報が全国がん登録データベースで一元管理されることとなった。これらの状況に鑑み、平成 27 年度の調査研究評価委員会において、放射線被ばくによる健康影響、特にがんの発生に及ぼす影響を評価する際、その評価指標としてがん罹患を新たに加えることを決定した。また、同委員会において、がん罹患情報を利用するために必要となる法的根拠、申請手続、全国がん登録データベース届出項目を確認するとともに、利用可能時期、疫学調査解析での利用法等について審議した。特に、がん罹患情報管理システムを開発するための要件定義として、全国がん登録データベースから提供を受ける

項目を確認した。

平成 28 年度には、調査研究評価委員会において、国における全国がん登録データベース整備の進捗状況、利用手続マニュアル等の整備状況等を報告するとともに、がん罹患リスクの評価に用いる臓器線量構築について検討を行った【「２．２ 臓器線量の再構築等の活用方策について」参照】。

平成 29 年度には、調査研究評価委員会において、全国がん登録データベースの利用申請方法等について検討を行った。

平成 30 年度には、調査研究評価委員会において、公開された診断年 2016 年全国がん登録情報の概要を報告し、利用方針についてより具体的に検討を行った。

令和元年度には、提供が開始された診断年 2016 年全国がん登録情報について、法第 17 条第 1 項第 3 号の規定に基づき「非匿名化情報」の利用申請を行い、承認後に疫学 DB とのリンケージを行った。調査研究評価委員会及びあり方検討会フォローアップ委員会では、公表された診断年 2016 年全国がん登録情報の精度、疫学 DB と全国がん登録データベースとのリンケージ結果データの集計方法等について検討を行った。

令和 2 年度には、前年同様、診断年 2016～2017 年全国がん登録情報について、利用申請を行い、承認後に疫学 DB とのリンケージを行った【巻末参考資料 25 頁 図１．３．１参照】。調査研究評価委員会等において、リンケージ結果データの集計方法及び集計結果等について検討を行った【巻末参考資料 25 頁 図１．３．２及び 26 頁 図１．３．３参照】。

２．１　全国がん登録情報の更新

診断年 2016～2018 年全国がん登録情報について、令和 3 年 5 月、当協会理事長から厚生労働大臣に対して利用申請を行った。6 月に全国がん登録情報の利用と提供に関する審査委員会、7 月にがん登録部会が開催され、9 月に応諾の通知を厚生労働大臣から受け取った。その後、疫学 DB と全国がん登録データベースをリンケージするために、リンケージ用外部照合データ約 26 万件を作成し、国立がん研究センターに送付した。リンケージの結果、がん罹患情報を付加したリンケージ結果データが提供された。リンケージ結果データに基づき、がん罹患情報 DB を更新した。

２．２ 臓器線量の再構築等の活用方策について

平成 27 年度以降の本疫学調査では、評価指標として従来の死亡に加え、平成 28 年に始まった全国がん登録制度のがん罹患情報を利用することとなった。これに伴い、線量については、従来、線量計等の記録線量である個人線量当量をそのままリスク推定に用いていたが、放射線リスク評価の国際比較可能性を高めるために、海外の放射線疫学調査で用いられている組織・臓器吸収線量を用いることとして、平成 29 年度及び平成 30 年度に臓器線量構築検討会を設置し、検討を行った。

平成 30 年度には、線量計レスポンスの試験の実施、日本人成人男性モデルの臓器線量換算係数の推計並びに日本の原子力発電所における光子エネルギー及びジオメトリ分布に関する先行研究の調査を経て、記録線量から組織・臓器吸収線量への換算係数を構築し、同検討会

報告書にとりまとめた。

令和元年度には、同検討会報告書の換算係数に基づき、第Ⅴ期（平成 22 年度～平成 26 年度）解析対象者について、1957～2010 年の記録線量から組織・臓器吸収線量への試算を行った。

令和 2 年度には、試算した組織・臓器吸収線量を用いて第Ⅴ期解析対象者について再解析を行い、従来の記録線量を用いた解析結果と同様に喫煙調整により放射線リスク推定値が下がる傾向を示すことを確認した。また、今後は記録線量以外に臓器吸収線量を用いたリスク解析を行うことから、解析システムにおいて、臓器線量構築検討会報告書で取りまとめた臓器線量換算係数を用いて、調査対象者の 14 組織・臓器（結腸、赤色骨髄、食道、胃、肝臓、胆嚢、脾臓、肺、膵臓、前立腺、膀胱、腎臓、脳、心臓）別の吸収線量を計算し、リスク解析に用いる線量を容易に選択できる機能を追加した。

令和 3 年度には、令和 2 年度に計算した組織・臓器吸収線量を用いて、第Ⅴ期解析対象者について部位別がん死亡リスクの再解析を行い、第 66 回 Health Physics Society 年次総会で学会発表を行い、また、Journal of Radiological Protection 誌に論文発表を行った。再解析結果は、臓器吸収線量を用いても先行研究（工藤他 2018 年）と同様のリスク推定結果が得られることを示し、このことは臓器吸収線量を用いたとしても、喫煙交絡は J-EPISODE にとってバイアス要因であることを示唆している。

また、福島第一原子力発電所緊急作業者が緊急作業に従事した際の記録線量（以下「緊急作業線量」という。）についても通常作業線量に含めて分析する方針が令和 2 年度調査研究評価委員会及びあり方検討会フォローアップ委員会において承認されたことから、緊急作業線量を臓器吸収線量に換算する前提として、中央登録センターにおいて実効線量として記録されている緊急作業線量を、指定解除記録【巻末参考資料 27 頁 １．３．４参照】を用いて外部・内部被ばく線量に分割する方法を検討し、日本放射線影響学会第 64 回大会において学会発表を行った。これによって、指定解除記録を利用する方法は有効であるとともに、指定解除記録がまだ中央登録センターにない者がいるという課題が判明した。また空気中 I-131/Cs-137 濃度比【巻末参考資料 27 頁 １．３．５参照】を用いて内部被ばく線量（預託実効線量）から I-131/Cs-137 別預託実効線量を推計する方法について検討し、第３回日本放射線安全管理学会・日本保健物理学会合同大会において学会発表を行った。これによって、I-131 及び Cs-137 による組織・臓器吸収線量（例えば、結腸吸収線量）換算係数が得られるが、推定値の不確かさが課題であることが判明した。

これらの検討を踏まえ、緊急作業線量から臓器吸収線量を構築する手法の確立を目的として、次の外部専門家 4 人で構成される「緊急作業線量の臓器線量構築に関する検討会」を設置し、年度内に 2 回開催した。

緊急作業線量の臓器線量構築に関する検討会　委員構成（五十音順、○：座長）

○甲斐　倫明　学校法人文理学園 日本文理大学 新学部設置準備室 教授

栗原　治　　国立研究開発法人 量子科学技術研究開発機構 放射線医学研究所

計測・線量評価部長
佐藤　薫　　国立研究開発法人 日本原子力研究開発機構 原子力基礎工学研究センター
放射線挙動解析研究グループ 研究主幹
辻村　憲雄　国立研究開発法人 日本原子力研究開発機構 核燃料サイクル工学研究所
放射線管理部 研究主席

本検討会では、当協会から、緊急作業における被ばくの状況、利用可能なデータ、年度別臓器吸収線量構築に当たっての検討課題について説明を行い、以下の議論を行った。また、今後引き続き検討を進めることが確認された。

- 本疫学調査（J-EPISODE）で利用可能なデータの入手経路及び利用する際の制約を明確にすること。内部被ばく線量について、利用可能なデータが評価結果である預託実効線量のみである場合は、その評価プロセスを可能な限り明確にすること。
- 協会の説明では預託実効線量を被ばくに寄与する核種ごとに分割する方法（以下「核種分割」という。）に関して、その対象を I-131 と Cs-137 のみとしているように見えるが、Cs-134 を追加するとともに、Cs-137 と Cs-134 の存在比が同程度であったことを明記すること。
- 核種分割に作業環境の空気中濃度比を用いる場合、それを利用することによる不確かさを評価すること。
- 実測データが存在しない短半減期核種について、考慮しなくてもよいと判断するための先行研究等の根拠について情報収集すること。
- 核種分割に作業環境の空気中濃度比を用いる場合、個人別に摂取日を考慮する必要がある。その際、指定日【巻末参考資料 27 頁 １．３．４参照】を摂取日と仮定する場合、指定日と実際の摂取日との違いが、どの程度臓器吸収線量に影響するのかを評価しておくこと。
- 臓器吸収線量の不確かさの評価について、複数の摂取シナリオ（例えば、I-131 が支配的な時期、I-131 と Cs（Cs-134 及び Cs-137）が同程度になった時期、I-131 の影響がなくなった時期等）を用いた感度分析的アプローチ等を別途検討すること。
- 外部被ばくでは、Cs-134、Cs-137、短半減期核種等の光子エネルギーに留意すること。また、使用された個人線量計タイプを確認すること。

３．委員会活動

３．１　放射線疫学調査 倫理審査・個人情報保護委員会

(1) 開催日：令和 3 年 12 月 9 日

(2) 委員構成（五十音順、○：委員長）

○浦川道太郎　学校法人 早稲田大学 名誉教授・弁護士
金野　朋博　株式会社日立製作所　原子力ビジネスユニット原子力事業統括本部
菊池　浩明　学校法人 明治大学 先端メディアサイエンス学科 教授
栗原千絵子　学校法人 神奈川歯科大学 特任教授
佐々木秀智　学校法人 明治大学 法学部　 教授
広田すみれ　学校法人 東京都市大学 社会メディア学科 教授
吉永　信治　国立大学法人 広島大学 原爆放射線医科学研究所 教授

(3) 委員研修

医学系研究倫理の専門家である栗原委員より、文部科学省、厚生労働省及び経済産業省（以下「3 省」という。）が令和 3 年 3 月に共同で制定し 6 月に施行された「人を対象とする生命科学・医学系研究に関する倫理指針」に基づき、旧指針類からの変更点及び本疫学調査への影響という観点から講義を受けた。委員からは同指針の要求事項や注意事項について理解が深まり、有意義な研修であったとの評価を得た。

(4) 議題

1) 報告事項
- 前回委員会の議論を踏まえた健康影響評価計画書の修正
- 今年度事業の進捗状況
- 韓国の個人情報保護法の動向

2) 審議事項
- 「人を対象とする生命科学・医学系研究に関する倫理指針」における学術研究の除外規定の協会への適用について

(5) 議事概要

1) 報告事項

現行の健康影響評価計画書は、平成 2 年度から始まった疫学調査のフレームワークが平成 27 年度から開始した第Ⅵ期調査では大きく変わることを受けて新たに策定したものであり、その骨子は調査対象者となることの意思確認を行うこと、死亡に加えて新たにがん罹患情報を利用すること等である。倫理指針では計画の策定と調査協力者に対して、その公表が求められている。前回（令和 2 年度）の本委員会における議論を踏まえ、海外との共同研究の可能性を考慮し、提供可能なデータを「統計データ」とより明確にした健康影響評価計画書の公表、今年度事業の進捗状況（生死追跡調査の進捗状況、がん罹患情報の活用状況、臓器線量変換作業の進捗状況、論文投稿及び学会発表）について事務局より報告した。また、韓国水力・原子力発電会社から平成 30 年度に提案のあった共同研究が韓国における個人情報保護法の改正に伴い中断となったことについて、韓

国における同法改正の動向とともに事務局より報告した。

委員からは、国内外での学会発表や論文投稿について国際的な業績が堅調であるとの評価を得た。また、韓国における同法改正は個人情報の二次利用に係る国際動向を反映したものであり、今後も継続的に動向を調査し、本委員会に報告するよう要請があった。

2) 審議事項

「人を対象とする生命科学・医学系研究に関する倫理指針」において学術研究機関に適用される除外規定（学術研究機関に対して、3 省が保有する個人情報の Opt-out でのデータ提供を可能とする規定）について、本疫学調査に適用される可能性ついて、3 省合同会議「生命科学・医学系研究等における個人情報の取扱い等に関する合同会議」資料を参考に審議を行った。

委員からは、令和 4 年度以降に公益法人等の研究所や学術研究を主たる目的として活動する機関が学術研究機関として認められる可能性が出て来たこと、学術研究機関と認定されるためには協会の定款に学術研究を事業としていることが記載されていることが望ましいが、そうでない場合には適切な準備をしておくのが望ましいこと、また 3 省のガイドラインの改定方針が定まる令和 4 年 4 月以降に 3 省の相談窓口等を通じて学術研究機関としてのオーサライズを得ることが望ましいとの指導を受けた。なお、当協会の定款には事業の一つとして「放射線影響に関する調査研究」と記載されていることを確認した。

３．２　放射線疫学調査 調査研究評価委員会

(1) 開催日：令和 4 年 2 月 10 日

(2) 委員構成（五十音順、○：委員長）

飯本　武志　国立大学法人 東京大学 環境安全本部 教授
岩崎　利泰　一般財団法人 電力中央研究所 サステナブルシステム研究本部 研究統括室 原子力(放射線安全)分野統括
兒玉　和紀　公益財団法人 放射線影響研究所　業務執行理事
○祖父江友孝　国立大学法人 大阪大学大学院 医学系研究科 教授
高田　千恵　国立研究開発法人 日本原子力研究開発機構 核燃料サイクル工学研究所 放射線管理部次長
椿　　広計　大学共同利用機関法人　情報・システム研究機構　統計数理研究所　所長
西本　　寛　ＪＡ長野厚生連佐久総合病院 総合医療情報センター長
吉永　信治　国立大学法人 広島大学　原爆放射線医科学研究所 教授

(3) 議題

1) 報告事項

・前回委員会の議論を踏まえた健康影響評価計画書の修正
・今年度事業の進捗状況
・がん罹患情報の取得

2) 審議事項

・緊急作業線量の取り扱い

(4) 議事概要

1) 報告事項

前回（令和 2 年度）の本委員会における議論を踏まえ修正した健康影響評価計画書の公表、今年度事業の進捗状況（生死追跡調査の進捗状況、臓器線量変換作業の進捗状況、論文投稿及び学会発表）並びにがん罹患情報の利用状況（令和 2 年度に取得した情報の集計結果及び令和 3 年度の利用申請状況）について事務局より報告した。

委員からは、がん罹患情報利用における悪性新生物に含まれない上皮内がんの取り扱いに関する長期的な検討の必要性について指摘を受けるとともに、がん罹患情報において過去の記録が更新された場合には最新の記録を用いて再度リンケージを行うことが確認された。統計法の改正により、個人情報を扱うためのセキュリティが確保された施設として総務省の承認を受け大学や行政機関に設置が認められたオンサイト拠点において、国の統計の調査票情報の利用が可能となった。このようなオンサイト拠点において人口動態調査死亡票の氏名を含むデータを利用できれば、死因情報のリンケージの利便性が増すことが期待される。当協会がこの拠点となることの可能性も含めて検討を行うこととした。

2) 審議事項

緊急作業線量の取り扱いについて、内部被ばく線量の不確かさの評価に関する検討が必要であるとの指導を受けた。本疫学調査で利用できる個人情報に制約はあるが、例えば、東京電力から緊急作業の状況について聞き取りを行い、論文として記録に残せないか等、緊急作業線量の臓器線量構築に関する検討会において検討すること、また、今後も「放射線業務従事者の健康影響に関する疫学研究」（NEWS）との情報共有を行うこととした。

３．３　放射線疫学調査 あり方検討会フォローアップ委員会

(1) 開催日：令和 4 年 3 月 14 日

(2) 委員構成（五十音順、○：委員長）

岡村　智教　学校法人慶應義塾 慶應義塾大学 医学部 衛生学公衆衛生学 教授
甲斐　倫明　学校法人文理学園 日本文理大学 新学部設置準備室 教授
祖父江友孝　国立大学法人 大阪大学大学院 医学系研究科 教授（欠席）
玉腰　暁子　国立大学法人 北海道大学大学院 医学研究科 教授
椿　　広計　大学共同利用機関法人 情報・システム研究機構 統計数理研究所 所長（欠席）
土居　主尚　国立研究開発法人 量子科学技術研究開発機構 放射線医学研究所 主任研究員
○吉村　健清　学校法人 産業医科大学 名誉教授

(3) 議題

1) 報告事項

・前回委員会の議論を踏まえた健康影響評価計画書の修正
・今年度事業の進捗状況
・がん罹患情報の取得
・厚生労働省によるミクロデータの研究公開事業について

2) 審議事項

・緊急作業線量の取り扱い

(4) 議事概要（主なもの）

1) 報告事項

前回（令和 2 年度）の本委員会における議論を踏まえ修正した健康影響評価計画書の公表、今年度事業の進捗状況（生死追跡調査の進捗状況、臓器線量変換作業の進捗状況、論文投稿及び学会発表）、がん罹患情報の利用状況（令和 2 年度に取得した情報の集計結果及び令和 3 年度の利用申請状況）並びに厚生労働省の人口動態調査の氏名付き調査票情報のオンサイト施設における利用の可能性について事務局より報告した。

委員からは、他機関との共同研究における統計データ（層別データ）以外のデータの提供、厚生労働省の人口動態調査の氏名付き調査票情報の利用、更には当該利用において当協会がオンサイト拠点となる可能性等について、積極的に検討を行うよう指示があった。

2) 審議事項

緊急作業線量の取り扱いについては、緊急作業線量の臓器線量構築に関する検討会報告書（令和 4 年度作成予定）を踏まえ、本委員会においても検討することとした。

４．本事業の理解促進活動

本事業の理解促進活動として、以下の学会発表、論文投稿等を行った。

４．１　ホームページによる放射線疫学調査関連情報の周知

令和 3 年度は以下の更新を行った。

更新日	更新内容
6/29	ニュースレターの掲載
6/29	日本産業衛生学会の発表要旨の掲載
10/12	Health Physics Society、日本放射線影響学会の発表要旨の掲載
10/12	Health Physics への論文掲載の告知
12/9	日本放射線安全管理学会・日本保健物理学会合同大会の発表要旨の掲載
12/9	Journal of Radiological Protection への論文掲載の告知
2/16	Health Physics、医学物理への論文掲載の告知、日本疫学会の発表要旨の掲載

４．２　国内外の論文投稿・学会発表

国内外の機関に積極的に引用される調査として専門家に認知されることを目的に、記録線量から臓器線量への変換に関する検討（学会発表⑤、論文③④）、緊急作業線量の取扱いに関する検討（学会発表③④）、全国がん罹患情報との照合に関する検討（学会発表①）、第Ⅴ期（平成 22 年度～平成 26 年度）調査対象者の疫学 DB を使用した最新の解析結果（学会発表②⑥、論文①）及び放射線疫学調査の総説（論文②）について、計 6 回の学会発表と 4 編の論文投稿を行った。（論文は全て公表済み。）

（１） 学会発表　（巻末参考資料 28～34 頁参照）

① 原子力施設作業者コホートと診断年 2016-17 年全国がん登録情報とのリンケージ結果. 第 32 回日本疫学会、web 発表、2022.1.27

② 階層モデルを利用した部位別がん死亡率解析：J-EPISODE. 第 3 回日本放射線安全管理学会・日本保健物理学会合同大会、web 発表、2021.12.2.

③ 緊急作業線量のリスク推定における取り扱い：J-EPISODE. 第３回日本放射線安全管理学会・日本保健物理学会合同大会、web 発表、2021.12.2.

④ 放射線業務従事者中央登録センターに定期線量報告された緊急作業線量の外部・内部被ばく線量への分割. 日本放射線影響学会第 64 回大会、web 発表、2021.9.23.

⑤ Reanalysis of Site Specific Cancer Mortality Using Reconstructed Organ Absorbed Dose: A Japanese Nuclear Facility Worker Cohort 1991-2010. 66th Annual Meeting of the Health Physics Society、web 発表、2021.7.28.

⑥ 放射線業務従事者における企業規模と累積線量、生活習慣の検討 第 94 回日本産業衛生学会、web 発表、2021.5.24

（２） 論文 （巻末参考資料 35～90 頁参照）

① A Risk Comparison between Lifestyle, Socioeconomic Status, and Radiation: A Cohort Study of Cancer Mortality among Japanese Nuclear Workers (J-EPISODE). Health Physics, 122, 2022. (ahead of print)

② 放射線業務従事者を対象としたコホート研究の総説. Jpn. J. Med. Phys. 41, 180-193, 2021.

③ Reanalysis of cancer mortality using reconstructed organ-absorbed dose: J-EPISODE 1991–2010. J. Radiol. Prot. 42, 011509, 2022.

④ Organ Dose Reconstruction Applicable for a Japanese Nuclear Worker Cohort: J-EPISODE. Health Physics. 121, 471-483, 2021.

（３） 階層マルコフ連鎖モンテカルロを使用した解析結果

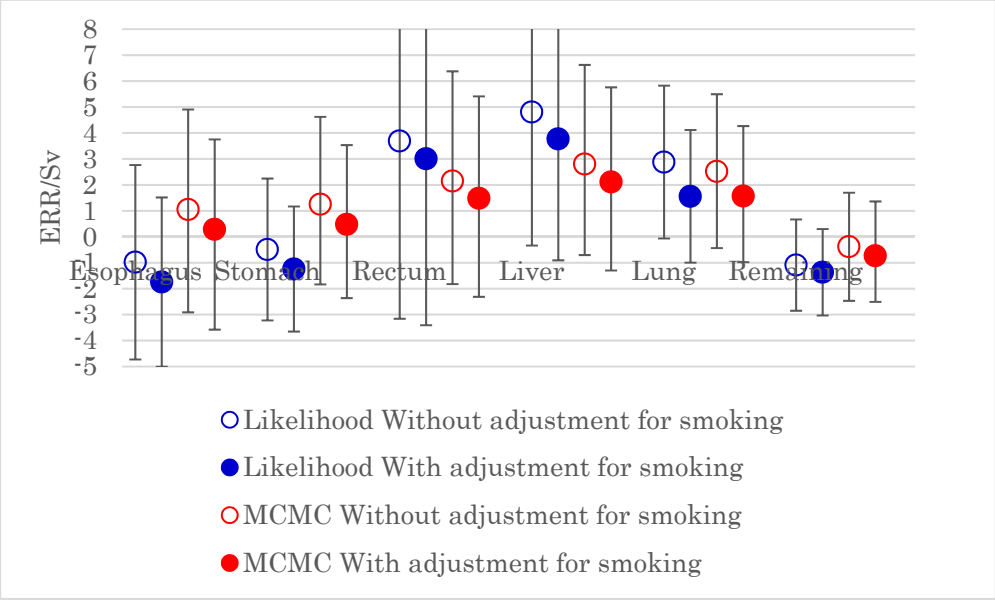
上記（１）学会発表、②「階層モデルを利用した部位別がん死亡率解析：J-EPISODE」の内容を以下に記す。

低線量・低線量率による健康影響を見るための放射線疫学調査では、白血病を除く全がんあるいは固形がんについて、最尤法によるポアソン回帰分析を適用することが多い。しかしながら、部位別のがんに着目した場合には、死亡数が少なくなることから、この最尤法を適用すると、例数の減少により推定精度が悪くなり、原爆被爆者の研究から得られている推定値に比べて極端に大きな、または小さな値となることがある。この問題を解決するため、INWORKS では部位別がん死亡率解析に階層マルコフ連鎖モンテカルロ（Hierarchical Marcov Chain Monte Carlo、以下 MCMC）を採用した。これは部位別の放射線リスク推定値について全体としておおよそ共通の値を取り得ると想定される一方、個体差も発生し得る場合にも対応できる方法であり、推定値のばらつきを抑えられ、信用区間（Credible interval、MCMC ではこう呼ぶ）も狭くできるという利点があり、INWORKS ではいずれも実現している。一方、J-EPISODE では喫煙調整によりリスク推定値が下がることが確認されている。ここでは J-EPISODE のデータを用いて MCMC を実施し、以下の 3 点を確認した。(1) 部位間の点推定値のばらつきを抑えられるか？ (2) 各部位の信用区間を（最尤法による信頼区間に比べて）狭くできるか？

(3)最尤法で見られた喫煙調整効果がMCMCでも見られるか？　(1)(2)はINWORKSで見られた結果の追試となるが、(3)はJ-EPISODE独自のポイントとなる。

解析対象者は1999年3月末までに放射線業務従事者として中央登録センターに登録された者のうち、1997年と2003年に実施した生活習慣等のアンケートにおいて喫煙状況が不明でない回答者とした。エンドポイントは死亡とし、生死の確認は住民票写しの取得により行った。死因は厚生労働省より提供を受けた、人口動態調査死亡票との照合により把握した。被ばく線量は中央登録センターから提供を受けた $H_p(10)$を用い、10年の潜伏期を仮定した。観察開始日はアンケート調査の回答から2年が経過した日とし、観察終了日は最終生死確認日、または2010年12月31日のいずれか早い方とした。

解析対象者は71,733人、総観察人年は59万人年であり、観察終了時の平均線量は25.5 mSvであった。死因毎のERR/Svを以下の図に示す。ここで青は最尤法の結果、赤はMCMCの結果であり、また、中抜きの円は喫煙調整前、塗りつぶしの丸は喫煙調整後であることを示す。



前述のチェックポイントの結果は次のとおりである。(1)MCMCでは部位間の点推定値のばらつきを抑えることができた。これは青のばらつきに比べて赤のばらつきが小さいことで確認できる。(2)直腸がん、肝がんでは信用区間を狭くできたが、その他の死因では不明瞭であった。(3)解析対象とした全ての死因で喫煙調整により、リスク推定値が下がった。これは中抜きの円に比べて塗りつぶしの丸が低いことで確認できる。

本研究ではINWORKSで見られた結果とほぼ同様の結果を得ることができた。また、喫煙調整効果が最尤法でもMCMCでも見られたことは、放射線疫学における交絡因子調整の重要性を示していると考えられた。

４．３　外部専門家との意見交換会

当協会が主催した、疫学調査の現状と課題に関する理解を深めることを目的とした令和 3 年度 ICRP 調査・研究連絡委員会「外部専門家との意見交換会」に参加し、「J-EPISODE における線量評価　～臓器線量の構築～」、及び「J-EPISODE における健康影響の解析　～交絡因子の調整～」の演題名で講演を行った。前者は $H_p(10)$で評価した実効線量から臓器線量への換算係数の構築方法、及び臓器線量による再解析結果について述べたものであり、今後の課題等について質疑応答を行った。後者はこれまでの解析における交絡の存在とその調整結果について述べたものであり、交絡の原因等について質疑応答を行った。

令和３年度原子力施設等防災対策等委託費

（低線量放射線による人体への影響に関する疫学的調査）事業

（原子力規制委員会原子力規制庁委託調査報告書）

（巻末参考資料）

目　　次

１．調査活動

表１．１　令和３年度　住民票の写し等の交付請求及び交付の状況（都道府県別）

都道府県名	申請		回答				取得率
	市区町村数	①件数	②住民票写し	③除票写し（転出）	④除票写し（死亡）	⑤該当者なし	②＋③＋④／①%
北海道	74	882	766	97	19	0	100.0
青　森	33	1,944	1,732	198	12	2	99.9
岩　手	24	90	81	4	5	0	100.0
宮　城	36	1,063	937	105	21	0	100.0
秋　田	17	68	64	3	1	0	100.0
山　形	19	51	47	1	3	0	100.0
福　島	44	3,334	3,040	202	90	2	99.9
茨　城	44	4,261	4,031	119	111	0	100.0
栃　木	20	164	155	6	3	0	100.0
群　馬	23	119	110	6	3	0	100.0
埼　玉	67	841	777	40	24	0	100.0
千　葉	52	965	899	39	27	0	100.0
東　京	50	1,616	1,439	133	44	0	100.0
神奈川	54	1,970	1,819	84	67	0	100.0
新　潟	33	821	752	51	18	0	100.0
富　山	12	175	165	6	4	0	100.0
石　川	16	519	455	57	7	0	100.0
福　井	17	1,672	1,539	103	30	0	100.0
山　梨	12	30	25	4	1	0	100.0
長　野	33	71	62	7	2	0	100.0
岐　阜	22	70	63	6	1	0	100.0
静　岡	36	751	678	56	16	1	99.9
愛　知	63	448	401	26	21	0	100.0
三　重	22	127	117	6	4	0	100.0
滋　賀	15	75	72	3	0	0	100.0
京　都	28	299	274	14	11	0	100.0
大　阪	69	778	694	55	29	0	100.0
兵　庫	42	1,118	1,015	55	47	1	99.9
奈　良	16	76	75	1	0	0	100.0
和歌山	14	41	40	1	0	0	100.0
鳥　取	15	111	102	8	1	0	100.0
島　根	11	606	534	65	7	0	100.0
岡　山	22	172	156	9	7	0	100.0
広　島	27	385	350	26	9	0	100.0
山　口	18	192	176	6	10	0	100.0
徳　島	13	34	30	3	1	0	100.0
香　川	16	137	125	10	2	0	100.0
愛　媛	17	609	564	40	5	0	100.0
高　知	10	31	27	3	0	1	96.8
福　岡	62	753	670	53	30	0	100.0
佐　賀	16	361	307	48	5	1	99.7
長　崎	17	175	163	8	4	0	100.0
熊　本	26	67	63	2	2	0	100.0
大　分	16	60	53	4	3	0	100.0
宮　崎	14	54	50	1	3	0	100.0
鹿児島	23	187	172	11	4	0	100.0
沖　縄	22	77	69	5	3	0	100.0
合　計	1,352	28,450	25,935	1,790	717	8	100.0

（本文　5 頁参照）

表１．２　同意者の生死追跡状況の詳細

令和4年 2月3日現在

群[注-1]	登録時期[注-2]	人数（総数）（男　女）	生死追跡状況の内訳		
			追跡結果	総数（男	女）
A－１	昭和63年度以前	36,932	生存	35,371	（ 35,370 1）
			死亡	1,550	（ 1,550 0）
		（ 36,931 1）	脱落	11	（ 11 0）
A－２	昭和63年度以前	3,365	生存	3,238	（ 3,237 1）
			死亡	119	（ 119 0）
		（ 3,364 1）	脱落	8	（ 8 0）
B	昭和63年度以前	1,184	生存	1,138	（ 1,138 0）
			死亡	44	（ 44 0）
		（ 1,184 0）	脱落	2	（ 2 0）
E	昭和63年度以前（燃料加工事業所のみの従事者および女子）	739	生存	714	（ 558 156）
			死亡	24	（ 21 3）
		（ 580 159）	脱落	1	（ 1 0）
C	平成1~6年度	15,205	生存	14,811	（ 14,641 170）
			死亡	378	（ 378 0）
		（ 15,035 170）	脱落	16	（ 16 0）
D	平成7~10年度	9,217	生存	9,032	（ 8,861 171）
			死亡	166	（ 164 2）
		（ 9,044 173）	脱落	19	（ 19 0）
F	平成27～30年度	14,865	生存	14,426	（ 14,087 339）
			死亡	82	（ 82 0）
		（ 14,520 345）	脱落	357	（ 351 6）
合計		81,507	生存	78,730	（ 77,892 838）
			死亡	2,363	（ 2,358 5）
		（ 80,658 849）	脱落	414	（ 408 6）
			（脱落の内訳）		
			住所不明等[注-3]		（ 408 6）
			不交付[注-4]		（ 0 0）

注－１ 第Ⅰ期放射線疫学調査解析対象：　Ａ－１
第Ⅱ期放射線疫学調査解析対象：　Ａ－１、Ａ－２、Ｂ、Ｅ、及びC
第Ⅲ期、Ⅳ期及び第Ⅴ期放射線疫学調査解析対象：　Ａ－１、Ａ－２、Ｂ、Ｅ、Ｃ、及びD
第Ⅵ期及びⅦ期放射線疫学調査解析対象：　Ａ－１、Ａ－２、Ｂ、Ｅ、Ｃ、D及びF

注－２ 放射線業務従事者として登録された時期

注－３ 調査対象者本人から入手した住所情報に基づいて行う生死追跡調査において、該当者なし、除票の保存期間経過、職権削除、海外転出等の理由により脱落した調査対象者の数

注－４ 市区町村の協力を得られなかったこと等により、住民票の写し等を取得できなかった調査対象者の数

１．３　がん罹患情報の取得

１．３．１　がん罹患情報のリンケージ

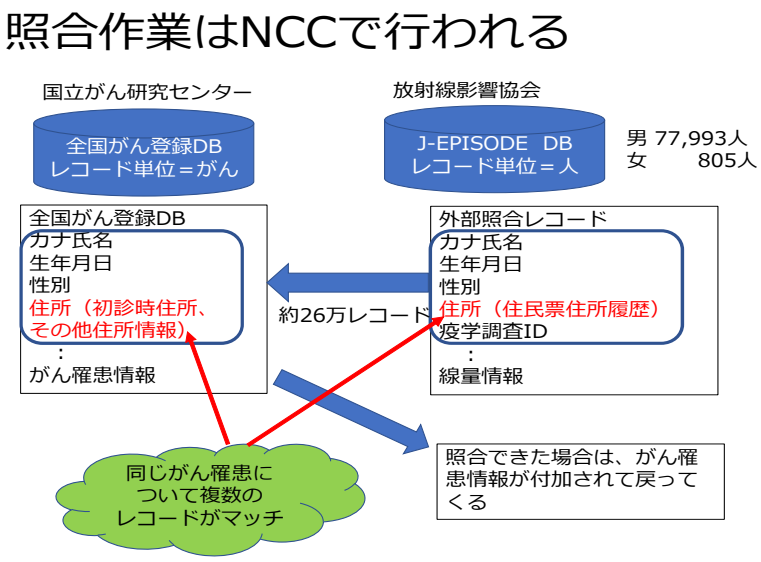


図１．３．１　全国がん登録 DB のレコードと J-EPISODE DB のレコードのリンケージ

１．３．２　がん罹患情報のリンケージ（照合）結果

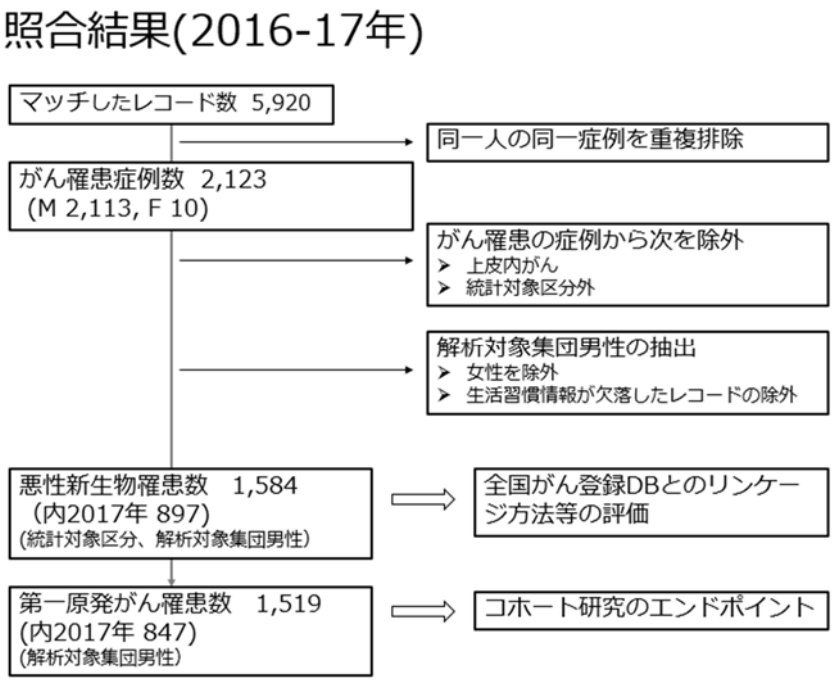


図１．３．２　リンケージの結果（2016～2017 年）

(注) 上記の数値は、全国がん登録法に基づき非匿名化情報の提供を受け、独自に作成・加工したものである。

１．３．３　がん罹患情報の集計結果

表１．３．３　部位、初診年齢、累積線量別第一原発がん罹患数
（診断年 2017 年、解析対象集団男性 77,993 人）

部位	罹患数	初診年齢（歳）					2015 年 3 月末累積線量(mSv)				
		-64	65-69	70-74	75-79	80+	<5	5-	10-	20-	50+
C16 胃	164	36	38	31	34	25	100	15	18	19	12
C18 結腸	69	21	10	14	13	11	48	6	6	4	5
C19-C20 直腸	51	16	14	7	8	6	34	3	5	5	4
C33-C34 肺	91	21	25	19	19	7	52	7	12	11	9
C61 前立腺	192	27	42	55	46	22	127	16	13	20	16
全部位合計	847	200	184	184	174	105	539	69	78	90	71

（注）罹患数が 30 以上の部位を表示した。

１．３．４　臓器線量の再構築等の活用方策に係る放射線業務従事者の指定解除記録

原子力事業者が中央登録センターに提出する線量データには 2 種類ある。1 つは、毎年度の個人別実効線量に関する定期線量報告データであり、これには外部・内部被ばく線量の内訳はない。もう 1 つは、当該原子力事業者における指定解除記録である。指定解除記録には、当該個人の指定年度前歴線量、当該原子力事業者における指定期間中の年度別、種類（外部、内部、皮膚、水晶体等）別線量等が記録されており、中央登録センターにマイクロフィルムの形式で保管されている。また、当該記録には、緊急作業線量についても、外部被ばく・内部被ばく別の線量が含まれており、一部の緊急作業者について指定解除記録の写しを取得することによって、緊急作業線量を外部被ばく線量と内部被ばく線量に分割できることを確認した。しかし、福島第一原子力発電所の緊急作業に従事してから現在までに従事者指定解除を行っていない者（従事者指定が継続している者）の指定解除記録は中央登録センターに保管されていない（指定解除後に提出される)。当該作業者について、類似の作業に従事した作業者の指定解除記録の写しから取得した外部・内部被ばく線量比を利用する方法を検討した。検討の結果、指定解除記録を利用する方法は有効であることが確認されたため、全ての緊急作業者の指定解除記録の写しを取得することとした。指定解除記録がまだ中央登録センターに保管されていない者の取り扱いについては今後検討することとした。

１．３．５　臓器線量の再構築等の活用方策に係る空気中 I-131/Cs-137 濃度比

預託実効線量を組織・臓器別吸収線量に変換する際には、まず核種別預託実効線量を推計する必要がある。例えば、I-131 は大部分が甲状腺に集積し、実効半減期が成人で約 7 日と短い。一方、Cs-137 は体内に均一に分布し、実効半減期が 30 歳で約 70 日、50 歳で約 90 日と長い。このように放射性核種によって摂取後の体内動態の相違から組織・臓器別吸収線量に及ぼす影響が異なるので、核種別の摂取量及び預託実効線量を推計する必要がある。本年度は、手法の検討として、主な放射性核種である I-131 と Cs-137 の吸入による摂取量の比率が作業場の空気中 I-131/Cs-137 濃度比に等しいとの仮定の下で、東京電力が測定した福島第一原子力発電所のダスト核種分析結果データ（東京電力平成 15 年 7 月 5 日プレスリリース）を利用して、I-131 と Cs-137 の核種別預託実効線量を試算した。

２．国内外への情報発信

２．１　学会発表

（１）第 32 回日本疫学会、web 発表、2022.1.27

OD-062

原子力施設作業者コホートと診断年2016-17年全国がん登録情報とのリンケージ結果

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(公財) 放射線影響協会 放射線疫学調査センター

【背景】放射線影響協会(REA)は国の委託により1990年から放射線業務従事者の健康影響に関する疫学調査(J-EPISODE)を実施している。線量は個人線量計の年度合算値がREA放射線従事者中央登録センターに登録されている。生死・住所変更は住民票取得により追跡し、エンドポイントは従来死亡であった。2015-19年度に全員同意者から構成される新しいコホートを設定した。

【目的】解析対象集団（男性）77,993人について、2016-17年全国がん登録データとのリンケージを行い、年齢、部位別がん罹患状況を把握して、がん登録DB及びリンケージ方法の評価を行った。

【方法】全国がん登録法第17条第1項第3号の規定に基づき、非匿名化情報の利用申請を行った。応諾通知の受領後、国立がん研究センター（NCC）でリンケージを行うため、解析対象集団について氏名・生年月日、性別、住所、データ識別番号からなる外部照合データを作成した。住所は住民票による生死追跡の際に把握した住所履歴情報を用い、同一人について複数の外部照合データを作成した。リンケージの結果、NCCから罹患情報を付加して提供されたデータについて、重複データ等を排除し、年齢、部位別がん罹患数を集計した。また、評価のため、厚労省「全国がん登録罹患数・率報告」（2016-2017年）の罹患率を基準とした標準化罹患比(SIR)を推計した。

【結果】解析対象集団男性の診断年2017年の第一原発がん罹患数は847件であった。診断年2016年のSIRは70%程度と低目であったが、2017年は90.5%となり、リンケージが適切に行われていることを伺わせた。

【結論】J-EPISODEの参加者について、全国がん登録データと適切にリンケージできることが確認でき、今後の追跡によって、放射線のがん罹患リスクが推定できることが明らかとなった。

【利益相反】無

（注）1. 本研究は原子力規制庁の委託事業として実施している。2. 本研究のがん罹患情報は、全国がん登録法に基づき情報の提供を受け、独自に作成・加工した資料である。

（2）第３回日本放射線安全管理学会・日本保健物理学会合同大会、web 発表、2021.12.2.

2C1-3

階層モデルを利用した部位別がん死亡率解析：J-EPISODE

Site-specific cancer mortality analysis by hierarchical model: J-EPISODE

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Shin'ichi KUDO[1)], Hiroshige FURUTA[1)], Noboru ISHIZAWA[1)], Shin SAIGUSA[1)]
放影協[1)]
Radiation Effects Association[1)]

【背景、目的】低線量低線量率による健康影響を見る場合、白血病を除く全がんあるいは固形がんについて、最尤法によるポアソン回帰分析を適用することが通常である。しかしながら、部位別のがんに着目した場合には、死亡数が少なくなることから、同じ最尤法を適用すると、例数の減少により推定精度が悪くなり、原爆被爆者の研究から得られている推定値に比べて極端に大きな、または小さな値となることがある。

この問題を解決するため、INWORKS では部位別がん死亡率解析に階層マルコフ連鎖モンテカルロ（以下 MCMC）を採用した。これは部位別の放射線リスク推定値について全体としておおよそ共通の値を取り得ると想定される一方、個体差も発生し得る場合にも対応できる方法であり、推定値のばらつきを抑えられ、信用区間（Credible interval、MCMC ではこう呼ぶ）も狭くできるという利点があり、INWORKS ではいずれも実現している。

放射線影響協会（以下、放影協）が国の委託により実施している放射線疫学調査 J-EPISODE では喫煙調整によりリスク推定値が下がることが確認されている。本発表では、このデータを用いて MCMC を実施した結果を報告する。チェックポイントは以下の 3 点である。(1) 部位間の点推定値のばらつきを抑えられるか？ (2) 各部位の信用区間を（最尤法による信頼区間に比べて）狭くできるか？ (3)最尤法で見られた喫煙調整効果が MCMC でも見られるか？ (1)(2)は INWORKS で見られた結果の追試となるが、(3)は J-EPISODE 独自のポイントとなる。

【方法】解析対象者は 1999 年 3 月末までに放射線業務従事者として放影協内にある放射線従事者中央登録センター（以下、中登センター）に登録された者のうち、1997 年と 2003 年に実施した生活習慣等のアンケートにおいて喫煙状況が不明でない回答者とした。エンドポイントは死亡とし、生死の確認は住民票写しの取得により行った。死因は厚生労働省より提供を受けた、人口動態調査死亡票との照合により把握した。被ばく線量は中登センターから提供を受けた $H_p(10)$を用い、10 年の潜伏期を仮定した。観察開始日はアンケート調査の回答から 2 年が経過した日とし、観察終了日は最終生死確認日、または 2010 年 12 月 31 日のいずれか早い方とした。解析には SAS の MCMC プロシジャを用いた。

【結果】解析対象者は 71,733 人、総観察人年は 59 万人年であり、観察終了時の平均線量は 25.5 mSv であった。前述のチェックポイントの結果は次のとおりである。(1)MCMC では部位間の点推定値のばらつきを抑えることができた。(2)直腸がん、肝がんでは信用区間を狭くできたが、その他の死因では不明瞭であった。(3)解析対象とした全ての死因で喫煙調整により、リスク推定値が下がった。

【結論】本研究では INWORKS で見られた結果とほぼ同様の結果を得ることができた。また、喫煙調整効果が最尤法でも MCMC でも見られたことは、放射線疫学における交絡因子調整の重要性を示していると考えられた。

※ 本調査は原子力規制委員会原子力規制庁の委託業務として実施した。

（３）第３回日本放射線安全管理学会・日本保健物理学会合同大会、web 発表、2021.12.2.

2C2-5

緊急作業線量のリスク推定における取り扱い：J-EPISODE

Treatment of emergency work doses in risk estimation: J-EPISODE

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Radiation Effects Association[1)]

【目的】放射線影響協会は、1990 年から放射線業務従事者を対象に、低線量放射線の健康影響調査(J-EPISODE)を行っている。J-EPISODE の第Ⅴ期解析（観察期間 1991-2010 年）は 2011 年 3 月の福島第一原子力発電所事故以前が対象であったので通常作業線量のみを分析対象としていたが、第Ⅵ期以降の線量は事故に伴う緊急作業に従事した期間を含むこととなる。一方、緊急作業線量は、通常作業線量とは線量限度が異なり、また、内部被ばく線量を含む。本研究は、調査における緊急作業者及び緊急作業線量の取扱い方針を検討することを目的とする。

【方法】通常作業線量に緊急作業線量を加えることによる影響を調べるため、調査集団に含まれる個々の緊急作業者に対して、当協会放射線従事者中央登録センターに登録された緊急作業線量を内部被ばく・外部被ばくに分割推計し、緊急作業者を含めないことにより生じるバイアスの影響、また、緊急作業線量を通常作業線量に合算することがリスク推計に与える影響等について分析した。

【結果】第１に、第Ⅵ期コホート(77,993 人)から緊急作業者を除外すると、累積線量分布(2018 年度末)の高線量群の人数割合が小さくなり、バイアスが生じた。また、第Ⅴ期追加解析(観察期間 1991-2012 年)の ERR/Sv（白血病を除く全がん死亡）は、緊急作業者を除外すると 20%増加した。したがって、緊急作業線量が通常作業線量とは態様が異なるという理由で、緊急作業者を調査対象から除外する方法は、リスク分析にバイアスをもたらす恐れがあり、適切ではないことがわかった。

第２に、集団線量(1957-2018 年度)でみると、緊急作業線量が占める割合は 6.4%に過ぎなかった。緊急作業線量のうち外部線量を通常作業線量に加えても第Ⅵ期対象者の累積線量分布(2018 年度末)はほとんど変わらなかった。通常作業線量のみを用いた第Ⅴ期追加解析(観察期間 1991-2012 年)の ERR/Sv（白血病を除く全がん死亡、累積線量ラグ 0 年）は、緊急作業線量を加えてもほとんど影響が見られなかった。したがって、第Ⅵ期以降の解析対象者の通常作業線量に緊急作業線量を合算しても、リスク分析には影響を与えないことが明らかとなった。

【考察】J-EPISODE の方針として、緊急作業に従事した者を解析対象に含めた上で、緊急作業線量を通常作業線量に合算した職業被ばくを用いてリスク解析を行うことが妥当であると結論付けた。今後は、緊急作業線量の外部線量及び内部線量について、臓器線量換算係数を構築し、既に作成した通常作業線量の臓器線量と合算した上で、放射線リスク推定を行う予定である。

【その他】利益相反なし。

本研究は原子力規制庁の委託事業として実施した。

（４）日本放射線影響学会第 64 回大会、web 発表、2021.9.23.

放射線業務従事者中央登録センターに定期線量報告された緊急作業線量の外部・内部被ばく線量への分割

Partitioning of emergency work doses reported annually to RADREC into external and internal doses

Background and aim: J-EPISODE, an epidemiological survey for nuclear workers, will conduct risk estimation by converting the recorded doses reported annually to the Radiation Dose Registration Center (RADREC) into organ-absorbed doses. Only the sum of external and internal doses (effective doses) has been reported annually for emergency work doses due to the Fukushima Daiichi Nuclear Power Plant accident. However, the organ-absorbed dose estimation needs disaggregation into external and internal doses.

Materials and methods: In addition to annual dose reports, ad-hoc reports on historical external and internal doses by type of normal or emergency work are submitted to RADREC after lifting the designation of a nuclear worker and are stored on microfilm. No such report is available for those who have been working still after the emergency work. Emergency work doses including internal doses were stratified by effective dose groups in FY2010 or FY2011, TEPCO's or contractors' employee; then, the sample participants were selected from each stratum. Retrieving their microfilms, the proportion of internal doses was calculated by stratum, which was applied to the effective doses of each individual emergency worker to estimate separately the external and internal doses.

Results: The estimated proportion of internal doses in 50+ mSv was 40% for TEPCO employees in FY2010 and 20% for contractors, but it was 0.3% and 11.7%, respectively, in FY2011. Next, individual organ-absorbed doses from emergency work will be reconstructed separately by external and internal doses.

This work was funded by the Nuclear Regulation Authority.

（５）66th Annual Meeting of the Health Physics Society、web 発表、2021.7.28.

Title: Reanalysis of Site Specific Cancer Mortality Using Reconstructed Organ Absorbed Dose: A Japanese Nuclear Facility Worker Cohort 1991-2010

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ABSTRACT

Background: Japanese Epidemiological Study on Low-Dose Radiation Effects (J-EPISODE) has analyzed health effects in association with photon exposure assessed in $H_p(10)$ up to now. It is under way to estimate cancer morbidity and mortality risk evaluated in organ absorbed dose in a newly designed cohort, the features of which were 1) all participants have agreed to participate in the study, 2) had a baseline information including smoking, education, job, etc. from lifestyle survey, 3) were able to follow-up vital status and underlying cause of death, 4) were able to obtain cancer incidence data by linkage with National Cancer Registry, and 5) smoking confounding was suggested in association between radiation and cancer death.

Aim: To describe reconstruction method of organ absorbed dose and to reanalyze site specific cancer mortality risk for J-EPISODE with follow-up 1991-2010.

Materials and methods: The reconstruction method of organ dose principally followed the approach adopted in the IARC 15-Country Collaborative Study. The recorded dose was converted to air kerma, further converted to organ-absorbed dose. The method was modified considering recent usage practice of dosimeters in Japan and body size of Japanese. Conversion coefficient was estimated for the selected 14 tissues/organs: the colon, red born marrow (RBM), oesophagus, stomach, liver, gall bladder, spleen, lungs, pancreas, prostate, bladder, kidneys, brain and heart. Following reconstruction of organ absorbed dose for J-EPISODE during 1957 to 2010, Poisson regression method was applied for estimating ERR (Excess Relative Risk) for cancer mortality.

Results: The conversion coefficients were approximately 0.8 Gy/Sv. The estimated ERRs/Gy for site specific cancer mortality were compatible with the previous analysis using the recorded dose Hp(10). Decreasing trends of risk estimates by adjustment of smoking did not change even when organ-

absorbed dose was used.

Conclusion: The main features concerning smoking confounding in the previous risk analysis were also found in the reanalysis results using the organ-absorbed dose. J-EPISODE risk analysis will mainly use the reconstructed organ-absorbed dose in the future.

This work was funded by Nuclear Regulation Authority, Japan.

（6）第 94 回日本産業衛生学会、web 発表、2021.5.24

OD16-2

放射線業務従事者における企業規模と累積線量、生活習慣の検討

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【背景・目的】企業規模により従事者の健康状況が異なることが報告されている。放射線影響協会では、放射線業務従事者を対象とした放射線の健康影響を調べるコホート調査を行い、調査の一環として行った生活習慣等アンケート調査により、企業規模（原子力施設で働いていた時の雇用企業の従業員数）、及び喫煙等のリスク因子の情報を取得した。本発表では累積線量とリスク因子との関連を企業規模別に検討した結果を報告する。

【方法】アンケート票は自記式とし、2015 年から 2018 年にかけてインフォームドコンセントを取得した者に回答を依頼した。1999 年 3 月末までに放射線業務に従事した経験を有する者のうち、2015 年 3 月末時点で生存している者については住所を把握していたため郵送により調査票を配布し、併せて原子力発電施設等への調査票の直接配布も行った。企業規模は 20 人以下、21 人以上 300 人以下、301 人以上の 3 群とし（以下、1 群から 3 群と呼ぶ）、検討対象のリスク因子は喫煙、飲酒、運動不足、野菜摂取不足、20 歳からの体重増加（10 kg 以上）、とした。年齢、累積線量は 2019 年 3 月 31 日時点のものを用い、区分は各々<50、50 ー、60 ー、70 歳以上、<5、5 ー、10 ー、20 ー、50 ー、100 mSv 以上とした。累積線量とリスク因子との相関については累積線量と年齢との交互作用が有意な場合は年齢別に、有意でない場合は年齢を調整した上で、Cochran Mantel Haenszel 統計量により有意性を判断した。

【結果】アンケート回答者のうち企業規模が不明である者を除外した 74,145 人を解析対象とした。平均年齢は 59.1 歳（中央値 60 歳）、平均累積線量は 15.5 mSv（中央値 1.4 mSv）であった。企業規模別の人数は 1 群から 3 群の順に（以下同様）10,853 名（15%）、18,153 名（24%）、45,139 名（61％）であり、1 群と 2 群は累積線量の増加と共に人数割合が増加した。現在喫煙者割合は 43%、36%、24％であり、1 群と 3 群は全ての年齢群において、2 群は年齢を調整した上で累積線量との有意な正の関連が見られた。現在飲酒者割合は 65%、67%、73％であり、全ての群において累積線量との有意な関連は見られなかった。定常的な運動をしない者の割合は 70%、66%、58％であり、全ての群において年齢を調整した上で累積線量との有意な正の関連が見られた。野菜をほとんど食べないと回答した者の割合は、8%、7%、4％であり、3 群において年齢を調整した上で累積線量との有意な正の関連が見られた。20 歳からの体重増加が 10 kg 以上の者の割合は 26%、27%、24％であり、1 群は累積線量との有意な関連は見られなかったが、2 群において年齢を調整した上で累積線量との有意な正の関連が見られた。また 3 群では 50 歳未満群と、70 歳以上群において累積線量との有意な正の関連が見られた。リスク因子の保有割合は企業規模により異なり、また累積線量との相関も野菜摂取不足や体重増加では企業規模により異った。これらの結果は企業規模により死亡率が異なることや、放射線リスクの検討に当たっては喫煙等の放射線以外のリスク因子を調整することが必要であることを示唆している。

※　本調査は原子力規制委員会原子力規制庁の委託業務として実施した。

２．２　論文発表

（１）A Risk Comparison between Lifestyle, Socioeconomic Status, and Radiation: A Cohort Study of Cancer Mortality among Japanese Nuclear Workers (J-EPISODE). Health Physics, 122, 2022. (ahead of print)

OPEN

Paper

A Risk Comparison between Lifestyle, Socioeconomic Status, and Radiation: A Cohort Study of Cancer Mortality among Japanese Nuclear Workers (J-EPISODE)

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Abstract—**The health effects of low-dose radiation exposure have been a source of controversy. One possible reason is that epidemiological studies that compare radiation risk with other factors, such as lifestyle or socioeconomic status, have been limited. The aim of this study is to conduct a comparison of the cancer risk of mortality between radiation, lifestyle habits (such as smoking), and socioeconomic status (such as years of education) among Japanese nuclear workers. We assembled a cohort of 41,742 male nuclear workers in Japan who answered a lifestyle questionnaire survey conducted during 2003–2004. To exclude systematic errors caused by missing values, we used multiple imputation and Poisson regression to estimate relative risks and confidence intervals for lifestyle habits, socioeconomic status, and radiation. The total person-y from 2005 to 2010 were 215,000. The mean age and cumulative dose were 54.9 y and 24.8 mSv (10-y lagged dose), respectively. Significantly high relative risks were determined for smoking, alcohol consumption, frequency of medical examination, breakfast intake, sleep, and body mass index. Further, significantly high relative risks of radiation were shown for lung cancer and smoking-related cancers. Since the simultaneous inclusion of radiation and non-radiation variables in the model for relative risk (RR) calculation means that the calculated radiation RR is the result of adjustment by other variables, the risk of cancer from low-dose radiation, if any, is less than smoking and probably less than other lifestyle factors.**

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Key words: cancer; epidemiology; radiation, low-level; risk estimates

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INTRODUCTION

THE HEALTH effects of high-dose radiation were made visible by studies on atomic bomb survivors (Pierce et al. 1996; Preston et al. 2003; Ozasa et al. 2012). While several studies have been carried out (Kudo et al. 2018a and b; Haylock et al. 2018; Leuraud et al. 2015; Richardson et al. 2015), consensus on the health effects of low-dose radiation has not been established. This suggests that if they exist, these effects are difficult to detect because they are probably less than the risks due to lifestyle or socioeconomic status. However, there is considerable anxiety among the public about the health effects of low-dose radiation, especially after the accident at the Fukushima Daiichi Nuclear Power Plant, and it is often discussed in the context of whether radiation risks exist or not. However, to understand this, a comparison with other lifestyle or socioeconomic factors could be informative. While some studies have reported the results of risk comparisons between radiation and smoking (Cahoon et al. 2017; Kreisheimer et al. 2003; Kudo et al. 2020; Gilbert et al. 2013), those between lifestyle, socioeconomic status, and radiation for individual causes of death remain limited.

Moreover, a cohort study of cancer mortality among Japanese nuclear workers in an epidemiological study on low-dose radiation effects (J-EPISODE: Japanese epidemiological study on low-dose radiation effects) has been conducted since 1990 by the Radiation Effects Association (REA). Information on lifestyle or socioeconomic status was obtained by a questionnaire survey for a part of the cohort, which consisted of 41,742 participants. However, there was some missing data (from 1 to 12% depending on the questions) in their responses. Thus, if a complete case analysis is done, the cohort will be reduced by 25%. In this case, a single imputation or complete case analysis revealed that the results were biased when the missing data did not occur completely at random. One of the solutions was multiple imputation (Rubin 1987; Rubin and Schenker 1991). We have previously compared the risk between death due to radiation and death due to smoking (Kudo et al. 2020). In the

present study, the variables for comparing risk are expanded to compare the risk of cancer death among more factors.

Thus, the aim of this study is to examine the comparison of mortality between lifestyle, socioeconomic status, and radiation for grouped cancers and site-specific cancers. This is accomplished by the simultaneous derivation of relative risks from one cohort by multiple imputation and Poisson regression.

MATERIALS AND METHODS

Ethical approval

The study protocol was based on the Ethical Guidelines for Medical and Health Research Involving Human Subjects by the Japanese Ministry of Education, Culture, Sports, Science and Technology, Ministry of Health, Labour and Welfare (MHLW).

Cohort definition and follow-up of vital status

The present study, J-EPISODE, is a prospective cohort study, and its endpoint was death. To this end, a mortality follow-up was carried out on those workers of Japanese nationality who were registered in the Radiation Dose Registry Center (RADREC) within the REA as of the end of March 1999.

To ascertain workers' vital status, copies of the residence registration cards (RRCs) were acquired from local government offices. These copies were issued when subjects were alive, and those of deleted RRCs, including death dates or new addresses, were issued when subjects were deceased or had moved away. Obtaining the informed consent of those included in the cohort was performed from 2007 to 2009. The refusal rate was approximately 7%. For those whose data we obtained but who later refused to participate, we ceased all follow-up efforts, and their observed period was censored on the last day on which their vital statuses were known.

To identify the causes of death among deceased participants, linkage with death records was approved for use and provided by MHLW. These records can almost completely ascertain the causes of death because they are based on the national registry. Indices used for record linkage were date of birth, date of death, sex, and municipality code of residence (Iwasaki et al. 2000). In the end, we were able to identify the cause of death for 99.5% of the subjects. The underlying causes of death were coded according to the International Classification of Diseases (ICD), 10th revision.

Dosimetry

The dose records were supplied by RADREC. Personal dose equivalent $H_p(10)$, which is the operational quantity of effective dose obtained from dosimeter readings, was used in the risk analysis. Here, the effective dose was the sum of the external and internal doses by fiscal year (from April to March of the next year). Moreover, external doses consisted of photons and neutrons. The photon doses were the external exposure records of equivalent doses at a tissue depth of 10 mm [$H_p(10)$]. In cases where neutron and internal doses were positively detected, they were added to external doses. However, such a case is so rare in Japan under routine nuclear work during normal operation, periodic inspections, and maintenance that those doses have little impact on the analysis.

The annual radiation exposure for each worker was calculated by adding doses from all facilities where they worked in a given year. Exposures below the detectable level were set as 0 mSv in the analysis. The present study covers radiation dose records from 1957—when the use of nuclear energy began in Japan—to the end of 2010, which was set as the censored date of the observation period.

Lifestyle questionnaire survey

To examine factors potentially confounding the risk assessment of nuclear workers, a lifestyle questionnaire survey was conducted from September 2003 to March 2004. It was given to a sample of male workers who were 40 y old or more as of 1 July 2003. The questionnaire was self-administered and included questions about lifestyle and socioeconomic status factors such as smoking, job category, years of education, and so on. The questionnaire was distributed by postal mail to all workers exposed to 10 mSv or higher radiation levels as of 31 March 2002, while 40% of workers with less than 10 mSv were sampled. However, the questionnaire was not distributed to female workers because the numbers of deceased females were too small to analyze (approximately 20). Therefore, female workers were excluded from the analysis, and questionnaires were distributed to 78,064 male workers.

Variables used for estimation of relative risks

The aim of this study was to estimate relative risk (RR) for each variable: smoking [pack-years (pack-y)], alcohol consumption (ethanol in g d^{-1}), health consciousness, frequency of medical examination, breakfast intake, sleep, body mass index (BMI), job category, position, years of education, and cumulative radiation dose. To compare with other studies, smoking was quantified as the total amount of smoking in pack-y for current smokers, while alcohol consumption was quantified as ethanol in g d^{-1} for current drinkers. The pack-y were defined as follows: the number of cigarettes per day $\times$ (1 pack/20 cigarettes) $\times$ the number of years between the age at which the individual started to smoke and the age on the survey date. RRs of current smokers were estimated by pack-y and defined against never smokers (those with 0 pack-y). In the case of former smokers, the mortality rate differs depending on the years since cessation of smoking. Because the model would be complicated if this were taken into account, the RRs of former smokers were not estimated by pack-y but estimated as

one former-smoker group against a group of never smokers. Meanwhile, ethanol in g d^{-1} was calculated by the type of liquor and frequency of drinking for current drinkers. RRs of current drinkers were estimated by ethanol in g d^{-1} against never drinkers (ethanol = 0 g d^{-1}). RRs of former drinkers were estimated as one former-drinker group against that of never drinkers. Finally, BMI was defined as an individual's weight (kg) divided by the square of height (m).

Causes of death

The causes of death for which RRs were estimated included all cancers excluding leukemia (hereafter "all cancers") (ICD10: C00–C90, C96–C97). Other causes included stomach cancer (C16), liver cancer (C22), colorectal cancer (C18–C21), lung cancer (C33–C34), smoking-related cancers (C00–C16, C22, C25, C30.0, C31–C34, C64–C67), and non-smoking-related cancers (C17–C21, C23–C24, C26–C29, C30.1–C30.9, C35–C63, C68–C80).

Multiple imputation

There were missing values in the answers to the lifestyle questionnaire. However, as they were not considered as missing completely at random, it was thought that the single imputation analysis or complete case analysis would be biased. Therefore, a multiple imputation method was adopted in three stages (Rubin 1987; Rubin and Schenker 1991) as shown below.

Imputation stage. A fully conditional specification was used for the imputation algorithm (*SAS* 2016). More specifically, conditional on the observed portion of the variable that contains missing data and the variable that does not contain missing data, an imputation model was constructed for each variable. Nominal variables—smoking status, alcohol consumption status, job category, and position—were based on discriminant function. Ordinal variables—health consciousness, frequency of medical examination, breakfast intake, sleep, and years of education—were based on ordinal logistic regression. Continuous variables—BMI, pack-y, and ethanol in g d^{-1}—were based on linear regression. Meanwhile, radiation doses from RADREC had no missing data. The following auxiliary variables without any missing data were included in the model to make the missing-at-random assumption more plausible: age at the time of the survey, number of sites where a worker has worked, the latest prefecture code that verified a worker's survival status, year of first exposure to radiation, and year of latest exposure to radiation. Further, indicators of death by all cancers were also added to the auxiliary variables as the endpoint.

An example of the imputation model of x_1 and x_2 when x_1 (e.g., pack-y) and x_2 (e.g., alcohol consumption) are missing is shown below:

$$x_1 = \beta_0 + \beta_2 x_2 + \beta_3 x_3 + \cdots + \beta_i x_i + \varepsilon$$

$$x_2 = \beta_0 + \beta_1 x_1 + \beta_3 x_3 + \cdots + \beta_i x_i + \varepsilon,$$

where x_1–x_i are the variables mentioned above, β_1–β_i are the parameters, β_0 is the intercept, and ε is the error term. When imputing x_1, x_2 is assigned by random sample from observed values as an initial value. Missing variable x_1 is estimated by the imputation model conditional on the other variables. When imputing x_2, the estimated parameters β_1 and x_1 are used as the condition for the imputation model. This process of estimating the parameters and the imputed values is repeated a certain number of times. However, the values at the beginning of the repeating process are discarded as "burn-in" because they may be affected by the initial value. In this way, multiple data sets (called pseudo-complete data sets) with imputed missing data are created. The number of burn-in was 100, and the created number of pseudo-complete data sets was 30 in this analysis. The MI procedure by SAS was used for imputation (SAS 2014, 2016).

Estimation stage. The entry date for person-year (person-y) calculations was set 2 y after the date of response to the questionnaire to prevent any health conditions at that time from affecting the analysis (Goodman et al. 1995). The exit date of the person-y calculation was set as whichever of the following was the earliest: (a) the date of the latest confirmation of vital status, (b) the date of death, or (c) 31 December 2010. Therefore, individual workers' observation periods differed, but they were within 2005 to 2010.

Next, to select a model for risk comparison, we examined the joint effect of smoking and radiation with reference to the studies of atomic bomb survivors (Pierce et al. 2003; Furukawa et al. 2010; Grant et al. 2017; Cahoon et al. 2017). The target cause of death was lung cancer, and the following Poisson regression models were used:

$$\lambda = \lambda_0(a, r)\exp(\alpha q)(1 + \beta_1 \cdot Smoke + \beta_2 \cdot Radiation + \gamma \cdot Smoke \cdot Radiation), \quad (1)$$

where λ is the death rate, and λ_0 is the background death rate [stratified by a: 5-y attained age categories (20–, 25–, ... and 100+); and r: residence, which is divided into eight regional categories within Japan (Kudo et al. 2018a and bb)]. Meanwhile, q is an indicator of a former smoker (1 = former smoker, 0 = current and never smoker), and α is a coefficient of q. However, calendar periods were not adjusted because the observation period was short (2005–2010). Meanwhile, "Smoke" refers to the pack-y for current smokers, and "Radiation" is the cumulative radiation dose. The unit of pack-y was 20 pack-y, and the unit of radiation was 100 mSv. Therefore, β_1 represents the smoking ERR per 20 pack-y, and β_2 represents the radiation ERR per 100 mSv. Here, it is worth noting that if the interaction term γ is significant, the joint effect of smoking and radiation is multiplicative; if not, it is additive. As a result of the

analysis, smoking was significant, radiation was not, and the interaction term was not significant (data not shown), suggesting that the joint effect is additive. Additionally, the simple additive model (2), simple multiplicative model (3), generalized additive model (4), and generalized multiplicative model (5) were used:

$$\lambda = \lambda_0(a,r)\exp(\alpha q)(1+\beta_1 Smoke+\beta_2 Radiation) \quad (2)$$

$$\lambda = \lambda_0(a,r)\exp(\alpha q)(1+\beta_1 Smoke)(1+\beta_2 Radiation) \quad (3)$$

$$\lambda = \lambda_0(a,r)\exp(\alpha q)(1+\beta_1 Smoke+\beta_2 Smoke\cdot Radiation) \quad (4)$$

$$\lambda = \lambda_0(a,r)\exp(\alpha q)(1+\beta_1 Smoke)(1+\beta_2 Smoke\cdot Radiation). \quad (5)$$

The results were mostly consistent with the common finding that smoking risk (β_1) was significantly high, but radiation risk (β_2) was not significant (Supplementary Table 1, http://links.lww.com/HP/A213). Since radiation was not significant, risk comparison seemed acceptable in both additive and multiplicative models, but when all 11 variables that are used for the estimation of relative risks as described in the above section were included in the model, the additive model did not converge. Consequently, the multiplicative model, which is easy to fit, was used in the following analysis.

Poisson regression was also used to quantify the RRs of lifestyle, socioeconomic status, and radiation based on the number of deaths and person-y after stratification according to the 5-year attained age categories and residence. Here, cumulative dose and attained age were treated as time-dependent variables. The former was lagged 10 y (Gilbert et al. 2013; Haylock et al. 2018; Kreisheimer et al. 2003; Kudo et al. 2018a, 2020; Richardson et al. 2015) and updated every month on the assumption that annual doses were distributed uniformly over each year. The model used to estimate relative risks was a log linear model, which implies multiplicative joint effects:

$$\lambda = \lambda_0(a,r)\exp(\beta_1 z_1 + \ldots + \beta_{11} z_{11}), \quad (6)$$

where z_1–z_{11} represent the variables that were used to estimate RRs. More specifically, z_1 was smoking (pack-y) defined as 0 (never smoker, reference; hereafter simply ref), former smoker, >0 (current smoker), 20– (current smoker), 40– (current smoker), and 60+ (current smoker). Former smoker was considered to be one category. Next, z_2 was alcohol consumption (ethanol in g d^{-1}) defined as 0 (never drinker, ref), former drinker, >0 (current drinker), 20– (current drinker), 40– (current drinker), and 60+ (current drinker). The former drinker was considered to be one category for the same reason as for the smokers mentioned above. z_3 was health consciousness defined as good (ref), medium, and bad. z_4 was frequency of medical examination defined as every year (ref), sometimes, and almost never. z_5 was breakfast intake defined as every day (ref), sometimes, and almost never. z_6 was sleep defined as well (ref), sometimes not well, and not well. z_7 was BMI defined as <18.5, 18.5– (ref), 25–, and 30+. z_8 was job category defined as design and research (ref), radiological management, operation and investigation, and maintenance. z_9 was position defined as management (ref), technical advisor, group leader, and staff. z_{10} was years of education defined as 13+ (ref), 10–12, and <10. Finally, z_{11} was the cumulative radiation dose assuming a 10-y lag defined as <5 (ref), 5–, 10–, 20–, 50–, and 100+ .

Meanwhile, β_1–β_{11} represent the coefficient–relative risk against these 11 reference categories, and 95% confidence intervals described below in the integration stage were calculated. The person-y table was created by DATAB, and the models were fitted by AMFIT. Both were EPICURE modules (EPICURE 2008).

Integration stage. Using the point estimates and variances for each RR calculated from the 30 pseudo-complete data sets described in the (1) imputation stage, we calculated the integrated point estimates, and 95% confidence intervals (CIs) of each variable and category were integrated by Rubin's method (Rubin 1987; Rubin and Schenker 1991) as shown below.

Integrated relative risk

$$\theta = \frac{1}{D}\sum_{d=1}^{D}\hat{\theta}_d,$$

where D is the number of pseudo-complete data sets (30 in this analysis), and $\hat{\theta}_d$ is the relative risk in each pseudo-complete data set. Thus, θ is the integrated relative risk—the arithmetic mean of the relative risks of pseudo-complete data sets.

Integrated variance:

$$T = W + \frac{D+1}{D}B$$

$$W = \frac{1}{D}\sum_{d=1}^{D}W_d$$

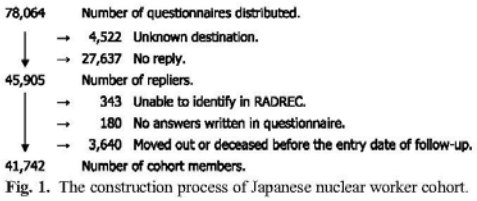

Fig. 1. The construction process of Japanese nuclear worker cohort.

Table 1. Number of subjects by each category of items among Japanese nuclear workers.

Items	Category	Number of subjects					
		Not imputed		PCD #1[a]		Complete case	
		41742	(100%)	41742	(100%)	31800	(100%)
Smoking	0 (Never, ref[b])	8494	(20%)	8790	(21%)	6889	(22%)
(Pack-y)	Former smoker	12555	(30%)	12975	(31%)	9802	(31%)
	>0	2134	(5%)	2159	(5%)	1733	(5%)
	20−	9595	(23%)	9864	(24%)	7635	(24%)
	40−	5508	(13%)	5728	(14%)	4130	(13%)
	60+	2197	(5%)	2226	(5%)	1611	(5%)
	Unknown[c]	1259	(3%)				
Alcohol consumption	0 (Never, ref[b])	6450	(15%)	7083	(17%)	5216	(16%)
[Ethanol / day (g)]	Former drinker	2660	(6%)	2885	(7%)	1808	(6%)
	>0	14881	(36%)	15563	(37%)	12591	(40%)
	20−	6715	(16%)	7624	(18%)	5725	(18%)
	40−	3605	(9%)	4209	(10%)	3100	(10%)
	60+	4129	(10%)	4378	(10%)	3360	(11%)
	Unknown[c]	3302	(8%)				
Health consciousness	Good (ref[b])	12690	(30%)	12884	(31%)	9521	(30%)
	Medium	26070	(62%)	26426	(63%)	20428	(64%)
	Bad	2399	(6%)	2432	(6%)	1851	(6%)
	Unknown[b]	583	(1%)				
Frequency of	Every year (ref[b])	33645	(81%)	34009	(81%)	26796	(84%)
medical examination	Sometimes	4865	(12%)	4951	(12%)	3276	(10%)
	Almost never	2742	(7%)	2782	(7%)	1728	(5%)
	Unknown[c]	490	(1%)				
Breakfast intake	Every day (ref[b])	34854	(83%)	35159	(84%)	26748	(84%)
	Sometimes	4044	(10%)	4069	(10%)	3061	(10%)
	Almost never	2499	(6%)	2514	(6%)	1991	(6%)
	Unknown[c]	345	(1%)				
Sleep	Well (ref[b])	24607	(59%)	24906	(60%)	19216	(60%)
	Sometimes not well	15211	(36%)	15389	(37%)	11580	(36%)
	Not well	1436	(3%)	1447	(3%)	1004	(3%)
	Unknown[c]	488	(1%)				
BMI	<18.5	1125	(3%)	1150	(3%)	782	(2%)
	18.5− < 25 (ref[b])	28872	(69%)	29104	(70%)	22125	(70%)
	25−	10496	(25%)	10596	(25%)	8227	(26%)
	30+	885	(2%)	892	(2%)	666	(2%)
	Unknown[c]	364	(1%)				
Job category	Design & research (ref[b])	3888	(9%)	4064	(10%)	3431	(11%)
	Radiological management	8034	(19%)	8379	(20%)	7170	(23%)
	Operation & investigation	5565	(13%)	5837	(14%)	4733	(15%)
	Maintenance	21800	(52%)	23462	(56%)	16466	(52%)
	Unknown[c]	2455	(6%)				
Position	Management (ref[b])	9945	(24%)	10535	(25%)	8956	(28%)
	Technical advisor	3940	(9%)	4361	(10%)	3358	(11%)
	Group leader	10201	(24%)	12201	(29%)	8434	(27%)
	Staff	12708	(30%)	14645	(35%)	11052	(35%)
	Unknown[c]	4948	(12%)				
Years of education	13+ years (ref[b])	12925	(31%)	13195	(32%)	11277	(35%)
	10−12 years	18940	(45%)	19670	(47%)	15416	(48%)
	<10 years	8236	(20%)	8877	(21%)	5107	(16%)
	Unknown[c]	1641	(4%)				
Radiation	<5 mSv (ref[b])	20353	(49%)	20353	(49%)	15435	(49%)

Continued next page

Table 1. *(Continued)*

Items	Category	Number of subjects					
		Not imputed		PCD #1[a]		Complete case	
(Cumulative dose)	5− mSv	2929	(7%)	2929	(7%)	2182	(7%)
	10− mSv	6259	(15%)	6259	(15%)	4747	(15%)
	20− mSv	6815	(16%)	6815	(16%)	5210	(16%)
	50− mSv	3429	(8%)	3429	(8%)	2704	(9%)
	100+ mSv	1957	(5%)	1957	(5%)	1522	(5%)

[a]Number of subjects of pseudo-complete data set #1. These were almost similar but differed slightly by data set.
[b]Reference category.
[c]The subjects classified under "unknown" were distributed to other categories by multiple imputation.

$$B = \frac{1}{D-1}\sum_{d-1}^{D}\left(\widehat{\theta}_d - \overline{\theta}_D\right)^2,$$

where T is the integrated variance, W_d is the variance of each pseudo-complete data set, and $\overline{\theta}_D$ is the arithmetic mean of relative risks of pseudo-complete data sets. These integrated relative risks and variances were calculated using the MIANALYZE procedure by SAS (SAS 2014, 2016).

Comparison with complete case analysis

There were 31,800 workers who responded to all the variables for calculating the relative risk. A complete case analysis was conducted against these respondents to compare with the results based on the multiple imputation for all cancers.

RESULTS

The process of cohort construction is depicted in Fig. 1. The lifestyle questionnaires were distributed to 78,064 workers. Of these, 45,905 workers replied, while the others were in unknown destinations and/or did not reply. In addition, the following were excluded: 1) unable to be identified in RADREC; 2) no answers written in the questionnaire; and 3) no follow-up period, such as those who moved or were deceased before the entry date of the follow-up (September 1, 2005). The remaining 41,742 workers were set as the cohort. Accumulated person-y were 215,000 through 2005 to 2010. The mean age and mean cumulative dose at the date of survey were 54.9 y and 24.8 mSv (10-y-lagged dose), respectively, while the mean duration of employment was 9.9 y. Table 1 shows the number of subjects by each variable before multiple imputation, after imputation (pseudo-complete data set #1), and a complete case analysis. The subjects who were in the unknown category were distributed to other categories by multiple imputation. Therefore, the number of subjects varied by each category and pseudo-complete data sets. Detailed numbers on the subjects are provided in Supplementary Table 2, http://links.lww.com/HP/A214.

Meanwhile, Fig. 2 shows the relative risks and 95% CIs by each cause of death and category of items. More specifically, significantly increasing RRs of all cancers, stomach cancer, liver cancer, lung cancer, and smoking-related cancers for smoking were seen (Panels A, B, C, E, and F). In these causes of death, dose responses—namely, as pack-y increased, RRs of smoking also increased—were also shown. Additionally, significantly increasing RRs of all cancers, liver cancer, colorectal cancer, and smoking-related cancers for alcohol consumption were seen (Panels A, C, D, and F). However, no significantly increasing RRs for health consciousness were seen. Moreover, significantly increasing RRs of all cancers, smoking-related cancers, and non-smoking-related cancers for frequency of medical examination were seen (Panels A, F, and G). Further, dose responses were seen in all cancers and smoking-related cancers (Panel A, F). Significantly increasing RRs of stomach cancer, colorectal cancer, and non-smoking-related cancers for breakfast intake were seen (Panels B, D, and G). The same was seen with that of liver cancer for sleep (Panel C) and all cancers for BMI (Panel A). However, there were no significantly increasing RRs for job category, position, and years of education. Significantly increasing RRs of lung cancer and smoking-related cancers for radiation were seen (Panel E, F). Finally, detailed relative risks and 95% CIs by each cause of death and category of items are described in Supplementary Table 3, http://links.lww.com/HP/A215. Results from the complete case analysis were different from those that were imputed (Table 2).

DISCUSSION

Principal findings

In this study, direct risk comparisons between lifestyle, socioeconomic status, radiation, and cancer mortality were examined. Lifestyle factors such as smoking, alcohol consumption, frequency of medical examination, breakfast intake, sleep, and BMI showed significantly increasing RRs. In particular, smoking showed greater RRs than other factors. In contrast, socioeconomic factors—such as job category, position, and years of education—showed no evidence of risk.

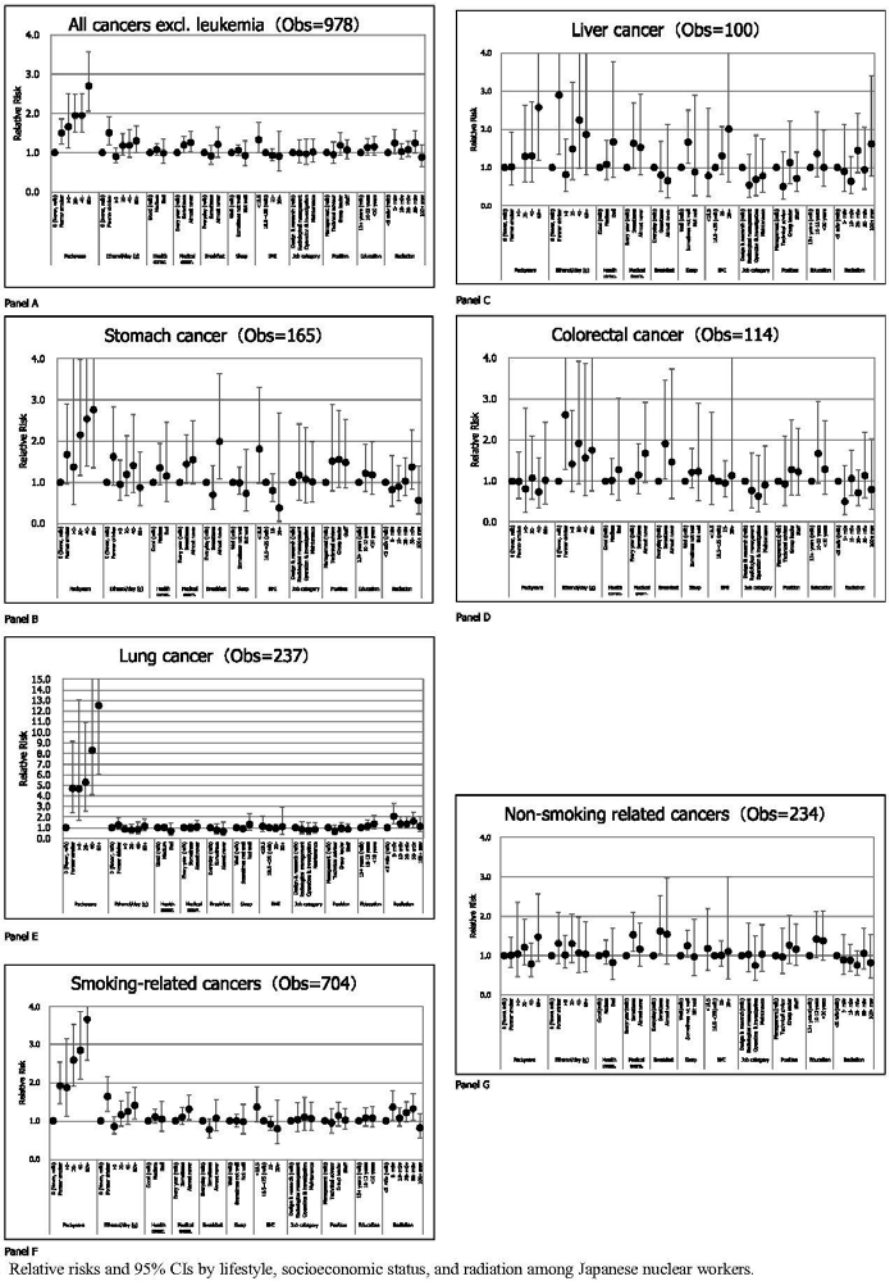

Fig. 2. Relative risks and 95% CIs by lifestyle, socioeconomic status, and radiation among Japanese nuclear workers.

Table 2. Relative risks and 95 % CIs for each category of items by imputed and complete case analysis for all cancers excluding leukemia among Japanese nuclear workers.

		Imputed		Complete case analysis	
Items	Category	RR (95%CI)		RR (95%CI)	
Smoking	0 (Never, ref[a])	1.00		1.00	
(Pack-y)	Former smoker	1.51	(1.22–1.86)	1.41	(1.14–1.76)
	>0	1.66	(1.11–2.50)	1.43	(0.92–2.23)
	20–	1.95	(1.53–2.49)	1.93	(1.50–2.47)
	40–	1.95	(1.53–2.50)	1.79	(1.39–2.30)
	60+	2.71	(2.05–3.57)	2.70	(2.04–3.58)
Alcohol consumption	0 (Never, ref[a])	1.00		1.00	
[Ethanol / day (g)]	Former drinker	1.51	(1.20–1.91)	1.94	(1.51–2.50)
	>0	0.90	(0.74–1.11)	1.07	(0.86–1.33)
	20–	1.18	(0.93–1.49)	1.34	(1.05–1.71)
	40–	1.19	(0.89–1.59)	1.35	(1.01–1.81)
	60+	1.30	(1.01–1.68)	1.52	(1.17–1.97)
Health consciousness	Good (ref[a])	1.00		1.00	
	Medium	1.08	(0.94–1.24)	1.19	(1.02–1.38)
	Bad	0.99	(0.72–1.35)	1.10	(0.79–1.54)
Frequency of	Every year (ref[a])	1.00		1.00	
medical examination	Sometimes	1.19	(1.01–1.41)	1.20	(1.00–1.43)
	Almost never	1.26	(1.02–1.55)	1.37	(1.10–1.70)
Breakfast intake	Every day (ref[a])	1.00		1.00	
	Sometimes	0.92	(0.71–1.18)	0.88	(0.67–1.16)
	Almost never	1.21	(0.89–1.65)	1.35	(0.99–1.82)
Sleep	Well (ref[a])	1.00		1.00	
	Sometimes not well	1.06	(0.93–1.21)	1.05	(0.92–1.21)
	Not well	0.93	(0.66–1.30)	0.94	(0.65–1.36)
BMI	<18.5	1.34	(1.01–1.77)	1.10	(0.78–1.55)
	18.5– < 25 (ref[a])	1.00		1.00	
	25–	0.94	(0.80–1.10)	0.95	(0.81–1.12)
	30+	0.91	(0.54–1.55)	1.03	(0.59–1.79)
Job category	Design & research (ref[a])	1.00		1.00	
	Radiological management	0.99	(0.74–1.32)	0.96	(0.73–1.26)
	Operation & investigation	0.97	(0.70–1.34)	0.97	(0.71–1.32)
	Maintenance	1.01	(0.77–1.34)	1.05	(0.81–1.36)
Position	Management (ref[a])	1.00		1.00	
	Technical advisor	0.96	(0.72–1.27)	1.01	(0.78–1.31)
	Group leader	1.19	(0.94–1.50)	1.14	(0.92–1.42)
	Staff	1.07	(0.86–1.33)	1.02	(0.83–1.25)
Years of education	13+ years (ref[a])	1.00		1.00	
	10–12 years	1.14	(0.94–1.37)	1.11	(0.93–1.33)
	<10 years	1.16	(0.94–1.42)	1.23	(1.00–1.50)
Radiation	<5 mSv (ref[a])	1.00		1.00	
(Cumulative dose)	5– mSv	1.25	(0.98–1.59)	1.04	(0.78–1.38)
	10– mSv	1.03	(0.85–1.24)	1.03	(0.84–1.25)
	20– mSv	1.08	(0.90–1.29)	0.99	(0.81–1.20)
	50– mSv	1.24	(0.996–1.55)	1.20	(0.95–1.52)
	100+ mSv	0.89	(0.65–1.20)	0.76	(0.55–1.06)

[a]Reference category.

Significantly increasing RRs of lung cancer and smoking-related cancers for radiation were also seen. The RR of category 5 mSv was 2.10 (95% CI: 1.34, 3.29), and the RR of category 50 mSv was 1.61 (1.03, 2.51) for lung cancer. These point estimates were larger than the RR for factors other than smoking but smaller than the RR for smoking—especially significantly lower than that for the 40 pack-y and over. Meanwhile, the RR of category 5 mSv was 1.35 (1.02, 1.80)

and the RR of category 50 mSv was 1.32 (1.02, 1.71) for smoking-related cancer. These point estimates were larger than the RR for factors other than smoking and alcohol consumption but smaller than the RR for smoking, the category of former drinker, and 60+ category of ethanol g^{-1} d^{-1} of alcohol consumption—especially significantly lower than that for ≥40 pack-y of smoking. Here, the comparison of radiation and smoking risk is unit-dependent, but these results suggest that the radiation risk, if any, is less than that of smoking. Further, our previous analysis comparing the risks of radiation and smoking in a larger cohort suggested that the radiation risk, if any, was less than the smoking risk (Kudo 2020). The present results are similar in this respect.

However, the results from complete case analyses were different from the imputed results to some extent. This probably reflected the fact that the multiple imputation was thought to be less biased than the non-imputed or complete case analysis. In addition, multiple imputation, which included auxiliary variables, made the assumption of missing-at-random more plausible and improved the precision of the analysis (Rubin 1987; SAS 2014).

Table 3 provides information on the observed and excess deaths of smoking and radiation by dose category and pack-y category for lung cancer and smoking-related cancers based on the pseudo complete data set #1. The model was a linear and multiplicative joint effect of smoking and radiation as follows:

$$\lambda = \lambda_0 \exp(\alpha_1 a + \alpha_2 r + \alpha_3 q)(1 + \beta_{1i} s_i)(1 + \beta_{2i} d_i), \quad (7)$$

where a is an attained age, r is residence, and q is an indicator of a former smoker (1 = former smoker, 0 = current and never smoker). Further, α_1–α_3 is a coefficient of a, r, and q; s_i is the pack-y category for current and never smokers (pack-y = 0); and d_i is the radiation dose category. Finally, β_{1i} and β_{2i} are coefficients of s_i and d_i, respectively.

Table 3 also shows the attributable fraction (AF), which is expressed as the proportion of excess to observed deaths. The AFs for lung cancer were 48%, 1%, and 2% for smoking only, radiation only, and smoking-radiation interaction, respectively. In this context, a study of atomic bomb survivors found that the AFs for solid cancer derived by males were 30%, 6%, and 2% (Grant 2017). Our results suggest that the AF of radiation may have been smaller because the average dose of the cohort was lower than that of the atomic bomb survivors, which in turn may have caused the AF of smoking to be relatively higher. In addition, the difference between our results for lung cancer and those of the atomic bomb survivors for solid cancers may also be a factor. For lung cancer, excess deaths of radiation only increased with increasing dose category, but conversely, it decreased for smoking-related cancers.

Comparison with other studies in terms of factors other than radiation

Mortality by several risk factors was also evaluated in the Japan Collaborative Cohort Study for Evaluation on Cancer (JACC) and the Japan Public Health Center-based prospective study on cancer and cardiovascular diseases (JPHC Study). The RRs for all cancers in the present analysis were compatible with the above studies for the most part. For example, the RRs of the 60+ category of pack-y in both the present analysis and the JACC were 2.71 (2.05, 3.57) and 2.48 (95% CI: 2.13, 2.90), respectively (Ozasa 2007a). The RRs of the 30+ category of pack-y in the present analysis and the JPHC were 1.95 (1.53, 2.49)

Table 3. Observed and excess death of smoking and radiation by dose category for lung cancer and smoking-related cancers based on pseudo complete data set #1 among Japanese nuclear workers.

Dose category (mSv)	Observed deaths	Background	Smoking only	AF smoking	Radiation only	AF radiation	Smoking-radiation interaction	AF smoking-radiation
Lung cancer								
<5	84	54.9	49.6	59%	0.0	0%	0.0	0%
5–	26	7.3	7.9	30%	0.1	0%	0.1	0%
10–	43	18.7	18.8	44%	0.3	1%	0.3	1%
20–	44	18.9	20.4	46%	0.7	2%	0.8	2%
50–	27	9.8	10.3	38%	0.8	3%	0.9	3%
100+	13	5.8	7.9	61%	1.1	9%	1.6	12%
Total	237	115.3	114.9	48%	3.1	1%	3.7	2%
Smoking-related cancers								
<5	291	215.9	112.3	39%	−0.1	0%	0.0	0%
5–	58	29.6	17.6	30%	−0.1	0%	−0.1	0%
10–	114	72.9	42.2	37%	−0.6	−1%	−0.3	0%
20–	135	75.4	45.5	34%	−1.4	−1%	−0.8	−1%
50–	75	38.4	23.0	31%	−1.5	−2%	−0.9	−1%
100+	31	23.7	17.2	55%	−2.1	−7%	−1.6	−5%
Total	704	455.9	257.7	37%	−5.8	−1%	−3.8	−1%

and 1.83 (95% CI: 1.34, 2.51), respectively (Hara et al. 2002). The RRs of the 60+ category of ethanol g^{-1} d^{-1} in the present analysis and the 81+ category of the JACC were 1.30 (1.01, 1.68) and 1.39 (1.20, 1.60), respectively (Ozasa 2007b). However, slightly higher RRs of smoking and alcohol consumption were seen in site-specific cancers in the present analysis relative to the JACC, although the CIs overlapped. The RRs of the 60+ category of smoking in the present analysis and the JACC were 2.76 (1.35, 5.62) and 1.57 (1.09, 2.25) for stomach cancer, 2.58 (1.20, 5.52) and 1.81 (1.14, 2.87) for liver cancer, and 12.52 (6.05, 25.90) and 7.85 (5.65, 10.9) for lung cancer, respectively (Ozasa 2007a). In addition, we found larger RRs of alcohol consumption in the present analysis than in the JACC. The RRs of the maximum category for liver cancer were 1.87 (0.82, 4.27) and 1.47 (0.96, 2.25) for the present analysis and JACC, respectively (Ozasa 2007b). Considering the difference in categories (the present analysis was 60+ and JACC was 81+), the RRs in the present analysis seemed higher. However, these discrepancies may be reflections of differences in cohort structure—the present analysis was based on an occupational cohort, and JACC and JPHC were based on an inhabitant cohort (Ohno et al. 2001; Hara et al. 2002). Moreover, the differences in age or baseline risk might contribute to this discrepancy. More specifically, significantly high RRs of alcohol consumption were shown for smoking-related cancer in the present analysis. This was likely because some cancers related to alcohol consumption were included in the smoking-related cancer category—for example, esophagus and liver cancers (Ozasa 2007a and b). Further, significantly high RRs were shown in the frequency of medical examination for all cancers, breakfast intake for stomach and colorectal cancers, sleep for liver cancer, and BMI for all cancers; however, the CIs of present analysis overlapped with the CIs of JACC (Suzuki 2007; Iso and Kubota 2007; Fujino 2007a).

Furthermore, significant differences in health effects by socioeconomic factors have been reported by some studies (Fujino 2007b; Kagamimori et al. 2009), but no significant differences were shown in this analysis. The cohort of this study was an occupation cohort. Thus, some differences between RRs of the present analysis and other studies were found, but their CIs overlapped. Therefore, the cancer mortality rates caused by lifestyle or socioeconomic status that were derived from our analysis could be regarded as compatible with other studies.

Comparison with other studies in terms of radiation

The CIs of radiation for all cancers that were derived from previous analyses overlapped with international nuclear worker studies for all cancers other than leukemia (Richardson et al. 2015), a UK national registry for radiation workers of all malignant neoplasms (excluding leukemia) (Haylock et al. 2018), and under 0.5 Gy categories of a study on atomic bomb survivors (Ozasa et al. 2012). Therefore, risk estimate on cancer mortality based on radiation, which was derived from our analysis, could be regarded as compatible with these studies.

Limitations

Some limitations of the present analysis should be acknowledged. First, the deficiency of statistical power is the greatest limitation. The total person-y were 215,000, and the number of observed deaths for all cancers was 978. These person-y and numbers of observed deaths might be insufficient for detecting risks by each variable and category, especially in site-specific cancer. Second, as shown in Fig. 1, the cohort of this study was the 41,742 respondents to the lifestyle questionnaire, but the number of those to whom the questionnaire was distributed was 78,064; the remaining 36,322 individuals did not respond. The mean ages of the 41,742 and 36,322 subjects in September 2003 were 54.9 and 53.7 y, respectively, and the mean radiation doses were 24.8 mSv and 20.9 mSv, respectively, with no significant difference between them. However, the fact that only about half of those who received the questionnaires responded to the survey suggests the existence of a potential bias. Third, there was a possibility that unadjusted confounding factors were present. Although dose response was not found, significantly high RRs of radiation were found in lung and smoking-related cancers. However, no significantly high RRs of radiation were found for non-smoking related cancers. These results may suggest that there are some unadjusted confounding factors related to both radiation and smoking.

CONCLUSION

The RRs of lifestyle, socioeconomic status, and radiation derived from this analysis were compatible with other studies. Despite the limitations, significantly high RRs of smoking, alcohol consumption, frequency of medical examination, breakfast intake, sleep, BMI, and radiation were found. Additionally, dose responses of RRs of smoking and frequency of medical examination were also found in the present analysis. Moreover, the results of this analysis showed that smoking is a major risk factor. Since the simultaneous inclusion of radiation and non-radiation variables in the model for RR calculation means that the calculated radiation RR is the result of adjustment by other variables, the risk of cancer from low-dose radiation, if any, is less than smoking and probably less than other lifestyle factors. The results offer worthwhile evidence in terms of the minimization of bias by using multiple imputation and estimation of RRs for several causes of death, variables, and categories from one simultaneous cohort.

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（2）放射線業務従事者を対象としたコホート研究の総説．Jpn. J. Med. Phys. 41, 180–193, 2021.

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解説

〈連載：教育委員会企画〉

放射線業務従事者を対象としたコホート研究の総説［第2部］

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Review of Cohort Studies Among Radiologists, Radiological Technologists, and Nuclear Workers

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A number of epidemiological studies have been conducted to investigate the health effects of low-dose radiation. The author reviewed epidemiological studies among radiologists, radiological technologists, and nuclear workers. Because the results of many epidemiological studies on these subjects have been published, and many studies have measured radiation doses, there is little uncertainty. In the studies among radiologists and radiological technologists, high risks for leukemia, skin cancer, and breast cancer were found in populations that began work before around 1950, but not seen such a tendency for those starting work recent years. The results of the studies among nuclear workers were inconsistent with some reporting that a risk was seen, while others reported no risk. The reason for this may be due to the different analysis methods among the studies.

Keywords: radiologist, radiological technologist, nuclear worker, occupational exposure, cancer

1. はじめに

1.1 背景，目的

高線量・高線量率放射線による組織反応，確率的影響については原爆被爆者の研究から明らかにされており，現在の放射線防護基準の基となるInternational Commission on Radiological Protection (ICRP)の勧告はこの結果に基づいている．一方，低線量・低線量率の放射線による健康影響については各国において様々な研究がなされている．低線量・低線量率放射線を被ばくした者に対する疫学研究には，高自然放射線地域の住民，CTスキャン受診者，放射線業務従事者等の研究があるが，放射線業務従事者は個人毎に線量が測定されているものが多く，これを対象とした研究は先の2つを対象とした研究に比べて不確かさが少ないと言える．またCTスキャン受診者は先に体調不良があるためにCTを受診するという因果の逆転が解析結果の解釈を困難にしており，従事者の研究はこの点でも不確かさは少ない．

疫学のデザインは大別すると，解析対象集団（以下，コホート）を設定して追跡を行うコホート研究と，研究開始時に過去に遡って死亡等の事象が発生した者と比較対照とする者の死亡率等を比較するケース・コントロール研究があるが，一般にはコホート研究の方が信頼性が高いと言われている．また，放射線業務従事者を対象とした疫学調査には航空機乗務員を対象としたもの[1)~3)]もあるが，多くの調査がなされているのはRadiologist（本稿では放射線科医），Radiological technologist, Radiographer（同，放射線技師），Nuclear worker（同，原子力従事者）を対象としたものである．本稿ではこれらをコホートとして放射線と健康影響との関連に着目した疫学研究を概括することを目的とした．

各研究は(1)コホート，(2)観察期間，総観察人年，(3)平均線量，(4)結果，の4項目で取りまとめた．各研究に触れる前に，研究を理解するための用語を1.2章で説明する．その後2章では放射線科医，放射線技師の研究を，3章では原子力従事者の研究を国別に取り上げ，4章で考察を述べる．2章の概要を表1に，3章の概要を表2にもまとめたが，同一コホートで複数の結果が発表されている場

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合，表では最近の結果，または代表的と思われる結果を取り上げた．

1.2 用語説明

1.2.1 総観察人年

個人毎の観察開始日（例えば従事開始日）から観察終了日（例えば死亡日）までの観察期間を，コホート全ての人数について足し合わせて，人年(Person–years)として表したもの．2人を3年観察した場合と3人を2年観察した場合はいずれも6人年となり，例えば年齢が20〜24歳の区分でこの両者の6人年が観察された場合，両者の年齢別死亡率は等しいと考える．コホートの年齢構成が違えば，総観察人年から算出される死亡率は異なるが，一般には総観察人年が多いほど解析結果の精度は上がり，統計量の信頼区間は狭くなる．なお，本稿では取り上げないが，原爆被爆者の研究における総観察人年は330万人年となっている[4]．

1.2.2 SMR, SIR, RR, HR

これらはいずれも着目する集団の死亡率（または罹患率）を対照集団と比べた時の比である．1であれば着目する集団の死亡率（または罹患率）は対照集団と等しいことを，また，信頼区間の下限値が1を超えれば有意に高く，上限値が1未満であれば有意に低いことを示す．例えば2であれば，着目する集団の死亡率（または罹患率）が対照集団の2倍であることを意味する．

SMR（Standardized Mortality Ratio，標準化死亡比）はコホートの死亡率を他の集団と比べる統計量として用いられる[5),6)]．SMRは次式の指標である．

SMR＝観察死亡数／期待死亡数

ここで観察死亡数は解析対象とする死因における死亡数であり，期待死亡数はコホートの死因・年齢・暦年等のカテゴリー別死亡率が対照集団の死亡率（多くはその国の男性全体または女性全体等の統計データ）と同率であると仮定した死亡数である．従事者は従事が可能である程度に健康であり，対照集団には健康状態が思わしくない者を含むことから，コホートが従事者である場合，SMRが1を大きく下回ることがあり，これを健康労働者効果(Healthy Worker Effect)と呼ぶ．コホートと比較のための対照集団の年齢構成，追跡期間の違いによる時代効果，ベースライン死亡率は各々の調査によって異なる．このためSMRの比較の際には，そのことを念頭に置く必要がある．

SIR（Standardized Incidence Ratio，標準化罹患比）はがん罹患数に着目した統計量で，SMRと同様に次式によって表される指標である．

SIR＝観察がん罹患数／期待がん罹患数

RR（Relative Risk，相対リスク）は着目する集団の死亡率を対照集団と比べた時の比という点でSMR，SIRと同義であるが，SMR，SIRが対照集団の死亡率を一般国民から求めることが多いのに対し，コホート内の別の集団を対照群とする場合にその比をRRとすることが多い．しかしその使い分けは厳密ではなく，放射線科医，放射線技師を対象とした調査では，健康労働者効果を避けるために被ばくの機会がほとんどない精神科医等を対照集団とし，対照集団と着目する集団の死亡率の比をSMRとしている研究もある．一方，それとは逆にSMR，SIRをRRと呼称している研究もある．本稿ではRRがSMR，SIRの意味で用いられている場合はSMR，SIRとし，表では解釈上差し支えなければ注釈を入れていない．

HR（Hazard Ratio，ハザード比）は着目する集団のハザード(注1)を他の集団のハザードで除したRRである．

1.2.3 ERR

ERR（Excess Relative Risk, 過剰相対リスク）は放射線疫学特有の統計量であり，単位線量当たりのコホートの死亡率（または罹患率．本章では以下同様）の増加分を表すために用いられる．定義はRR－1であり，RRは線量がゼロの場合に対する単位線量（多くは1 Sv）当たりの死亡率の比を示す[7)]．ゼロであれば着目する集団の死亡率は線量がゼロの集団と等しいことを，信頼区間の下限値がゼロを超えれば有意に高く，上限値がゼロ未満であれば有意に低いことを示す．解析に用いられた線量が実効線量ならERR/Sv, 臓器吸収線量ならERR/Gyと表される．ERR/SvまたはERR/Gyが2であれば，1シーベルトを被ばくした場合に，線量がゼロの場合と比べて死亡率が2倍上乗せされる，即ち死亡率が3倍となることを意味する．リスクが直線的に増加することを仮定した場合には（ほとんどの場合がそうである），例えば100 mSvの死亡率はERR/Sv(Gy)を10分の1にすることで求められる．エンドポイントががん罹患の場合でも表示は同じであるため，いずれであるのかは論文から読み取る必要がある．

統計量については，放射線科医，放射線技師の研究ではSMR, SIRが主に用いられている．ERRは線量データを必要とするが，これらの研究では線量が測定，推定されていないことが多いことを反映していると思われる．線量が測定（一部は推定）されている原子力従事者の研究ではERRが主に用いられている．

解析対象死因については，放射線科医，放射線技師の研究では主に全がん，全白血病が対象とされているが，原子力従事者の研究では主に白血病を除く全がん，慢性リンパ性白血病（Chronic lymphocytic leukemia, 以下CLL）を除く白血病が対象とされている．

(注1) 単位時間当たりのイベント数（ここでは死亡とする）という点で死亡率と同義であるが，この時間tを短くし$\Delta t \to 0$の極限を取ったものをハザードという．別の言い方をすれば，時間tまで生存していた者が次の瞬間に死亡する確率となる．

Table 1 Summary including SMRs and 95% confidence intervals of each epidemiological study of cancer mortality among radiologists and radiological technologists

Cohort[a]	Cohort size[b]	Observed period	Total PY[c]	Mean dose (mSv, mGy)	SMRs and 95% CIs					
					All causes	All cancers	Leukemia	Breast	Skin	Others
Japanese technologists [8]	12,195 (0)	1969–1993	272,043	Year of birth ≦1933: 470 mSv >1934: 132 mSv	Year of birth ≦1933: 0.69 (0.65, 0.74) >1934: 0.54 (0.46, 0.61)	Year of birth ≦1933: 0.81 (0.73, 0.90) >1934: 0.80 (0.63, 0.99)	Year of birth ≦1933: 1.55 (0.85, 2.60) >1934: 0.95 (0.35, 2.08)		Year of birth ≦1933: 1.58 (0.24, 5.73) >1934: 0.00 (0.00, 8.89)[d]	Lymphoma[e] Year of birth ≦1933: 1.59 (1.12, 2.20) >1934: 0.86 (0.40, 1.64)
US radiologists [13]	6,510 (0)	1920–1974	573,395		1.20	1.31	1.67			Non-cancers: 1.18
US radiologists [14]	43,763 (20)	1979–2008			Year of graduation (Male) <1940: 0.96 (0.88, 1.05) 1940–: 0.98 (0.93, 1.03) 1960–: 0.87 (0.81, 0.95) 1980+: 0.66 (0.54, 0.81)	Year of graduation (Male) <1940: 1.12 (0.94, 1.34) 1940–: 0.99 (0.90, 1.08) 1960–: 0.96 (0.84, 1.10) 1980+: 0.96 (0.62, 1.48)	Year of graduation (Male) <1940: 1.91 (0.83, 4.41) 1940–: 1.31 (0.89, 1.94) 1960–: 0.91 (0.52, 1.58) 1980+: 1.25 (0.17, 9.49)		Year of graduation (Male) <1940: 6.38 (1.75, 23.20) 1940–: 1.29 (0.78, 2.14) 1960–: 0.67 (0.37, 1.23) 1980+: 0.31 (0.04, 2.75)	Non hodjikin lymphoma Year of graduation (Male) <1940: 2.69 (1.33, 5.45) 1940–: 1.01 (0.70, 1.55) 1960–: 0.94 (0.58, 1.55) 1980+: 0.57 (0.11, 2.86)
US technologists [15]	146,022 (73)	1926–1997	698,028 [16]	37 mGy[f] [17]		Year of first worked <1940: 1.28 (0.93, 1.69)[g] 1940–: 1.17[g] 1950–: 1.18[g] 1960+: 1.00[g] (Reference)	Year of first worked <1950: 1.64 (0.42, 6.31)[g] 1950+: 1.00[g] (Reference)	Year of first worked <1940: 2.92 (1.22, 7.00)[gh] 1940–: 2.44 (1.26, 4.75)[gh] 1950–: 1.24 (0.77, 2.00)[g] 1960+: 1.00[g] (Reference)	Year of first worked <1940: 8.6 (1.0, 72.7)[gi] 1940–: 1.6 (0.5, 5.1)[gi] 1950–: 1.1 (0.5, 2.5)[gi] 1960–: 0.9 (0.5, 1.4)[gi] 1970+: 1.00[gi] (Reference) [16]	
US army technologists [24]	6,560 (0)	1946–1974	174,500		NS					
UK radiologists [25]	2,698 (0)	1897–1997	69,615		Year of first registration 1897–: 0.97 1921–: 0.92 1936–: 1.00 1955+: 0.68[j]	Year of first registration 1897–: 1.75[j] 1921–: 1.24 1936–: 1.12 1955+: 0.71			Year of first registration 1897–: 4.35 1921–: 4.55 1936–: 0.00[d] 1955+: 0.00[d]	
Canada [27]	67,562 (65)	1951–1987		3.78 mSv	0.53 (0.51, 0.55)[k]	0.78 (0.75, 0.82)[kl]				Thyroid cancer 1.74 (1.40, 2.14)[kl]
China x-ray workers [29]	27,011 (20)	1950–1995	694,886	Year of employed <1970: 551 mSv 1970+: 82 mSv		Year of employed <1970: 1.24[hl] 1970+: 1.08[l]	Year of employed <1970: 2.37[hl] 1970+: 1.73[l]	Year of employed <1970: 1.34[l] 1970+: 1.33[l]	Year of employed <1970: 4.31[hl] 1970+: 2.74[l]	
Denmark [30]	4,151 (82)	1968–1985	49,553	18.4 mSv		Year of radiation dose mesurement 1–: 1.04[l] 3–: 0.92[l] 6+: 1.21[l]		Year of radiation dose mesurement 1–: 1.21[l] 3–: 1.26[l] 6+: 1.43[l]		Prostate cancer 6.02 (1.94, 14.06)[l]

a: The number in blankets indicate the reference number. b: The number in parentheses indicate the percentage of women. c: Person years. d: The number of observed death was zero. e: Lymphatic and hematopoietic. f: Female breast dose. g: RR. h: $p<0.05$. i: Melanoma. j: $p<0.001$. k: 90% CI. l: SIR.

Table 2　Summary including ERRs, SMRs and 95% confidence intervals of each epidemiological study of cancer mortality among nuclear workers

Cohort[a]	Cohort size[b]	Observed period	Total PY[c]	Mean dose (mSv, mGy)	ERRs and 95% CIs				SMRs and 95%CIs
					All cancers excluding leukemia	Leukemia excluding CLL	Lung	Non-cancers	
Japan [33]	71,733 (0)	1999–2010	591,000	25.5	0.29 (− 0.81, 1.57)[d]	− 2.00 (− 5.68, 1.68)[de]	0.94 (− 1.24, 3.90)[d]	1.28 (− 0.03, 2.79)[d]	
US NPP[f] [34]	53,698 (12)	1979–1997	698,051	25.7	0.51 (− 2.01, 4.64)[g]	5.67 (− 2.56, 30.4)	0.246 (< − 2.51, 8.44)	6.40 (2.29, 12.2)	Solid cancers: 0.65 (0.59, 0.72) Non − cancers: 0.34 (0.32, 0.36)
US pooled [35]	119,196 (20)	1944–1991	4,019,065	20.2	0.14 (− 0.17, 0.48)	1.7 (− 0.22, 4.7)	0.069 (− 0.43, 0.66)	0.026 (− 0.25, 0.32)[h]	
US million worker [43]	1,028,301 (20)								
UK [46]	167,003 (10)	1955–2011	3,684,391	25.3[i]	Mortality: 0.285 (0.06, 0.53)[d] Incidence: 0.283 (0.10, 0.48)[d]	Mortality: 1.712 (0.06, 4.29)[d] Incidence: 1.782 (0.17, 4.36)[d] [47]	Mortality: 0.028 (− 0.38, 0.51)[d] Incidence: 0.13 (− 0.28, 0.61)[d]	Mortality: 0.251 (0.03, 0.49)[dj] [47]	All causes: 0.83 (0.81, 0.84) All cancers: 0.84 (0.82, 0.86) [47]
France [48]	59,004 (13)	1968–2004	1,469,949	18.4	0.36 (− 0.42, 1.25)[de]	3.52 (< 0, 16.00)[d]	0.81 (− 0.72, 2.78)[d]	0.31 (− 0.71, 1.52)[dj]	All causes: 0.60 (0.59, 0.62) Solid cancers: 0.68 0.65, 0.71) Pleural cancer: 1.69 (1.22, 2.27) Skin melanoma: 1.40 (1.02, 1.88)
Russia [49]	25,757 (25)	1948–2015	998,048	419[k]	0.12 (0.03, 0.21)[l] [50]	1.0 (0.5, 2.0)[d] [51]	Gamma: 0.164 (0.043, 0.300) Plutonium: 3.472 (1.534, 8.952) (Male)	0.04 (− 0.00, 0.09)[j] [52]	
Canada [53]	45,316 (17)	1956–1994	613,648	21.64	1.20 (− 0.73, 4.33)	9.79 (< − 1.49, 107)	3.13 (− 0.45, 10.4)		
Germany [56]	8,972 (3)	1991–2008	130,737	29.5	0.999 (0.996, 1.001)[m]	1.004 (0.997, 1.011)[m]	0.996 (0.990, 1.002)[m]	1.001 (0.999, 1.002)[m]	All causes: 0.50 (0.45, 0.56) All cancers: 0.65 (0.51, 0.82)
Korea (Mortality) [57]	79,679 (13)	1992–2004	633,159	6.1	7.2 (− 5, 21)[dn]	16.8 (− 34, 149)[do]	− 2.5 (− 6, 38)[d]		All causes: 0.58 (0.54, 0.62) All cancers: 0.73 (0.64, 0.82)
Korea (Incidence) [58]	8,429 (0)	1992–2005	63,503	19.9	2.06 (− 1.91, 9.0)		− 0.58 (< − 9.28, 19.59)[p]		All cancers: 1.07 (0.87, 1.30)[q] Thyroid: 5.93 (2.84, 10.9)[q]
15-country [59]	407,391 (10)	1943–2000	5,192,710	19.4	0.97 (0.27, 1.80)[d]	1.93 (< 0, 7.14)[d]	1.86 (0.49, 3.63)[d]	0.24 (− 0.23, 0.78) [60]	
INWORKS [62]	308,297 (13)	1944–2005	8,221,032	20.9[r]	0.48 (0.20, 0.79)[d]	2.96 (1.17, 5.21)[d] [63]	0.56 (0.08, 1.02)[d] [64]	0.19 (0.07, 0.30)[d] [65]	

a: The number in blankets indicate the reference number. b: The number in parentheses indicate the percentage of women. c: Person years. d: 90% CI. e: Last estimate. f: Nuclear Power Plant. g: Solid cancers. h: Cardiovascular diseases. i: 10-year-lagged dose. j: Circulatory disease. k: External lung dose. l: Solid cancers other than lung, liver, and bone. m: Hazard ratio per mSv. n: All cancers. o: All leukemia. p: No convergence of lower bound. q: SIR. r: Colon dose.

2.　放射線科医，放射線技師

2.1　日本：放射線技師[8),9)]

(1) コホート

1950年以前に生まれた日本の放射線技師12,195人（全て男性）．日本では線量計の装着が義務付けられたのが1958年であるため[10)]，それ以前に従事した可能性の有無により，コホートを1933年以前に生まれた者（コホート1：4,595人）と1934年以降に生まれた者（コホート2：7,600人）に分割した．

(2) 観察期間，総観察人年

1969～1993年，272,043人年．

(3) 平均線量

コホート1のうち職歴が入手できた3,461人の平均累積線量は470 mSvであった．コホート2については職歴が得られなかったが，21歳から60歳まで一般の病院で通常

の防護服を着用して勤務していたとの仮定に基づき132 mSvと推定された.

(4) 結果

日本人男性を対照としたSMRはコホート1, 2各々で, 全死亡では0.69 (95%信頼区間（以下, CI): 0.65, 0.74), 0.54 (0.46, 0.61), 全がんでは0.81 (0.73, 0.90), 0.80 (0.63, 0.99)と有意に低く, 健康労働者効果の可能性が考えられた. 白血病のSMRは各々1.55 (0.85, 2.60), 0.95 (0.35, 2.08)と点推定値に違いが見られ, リンパ造血系では1.59 (1.12, 2.20), 0.86 (0.40, 1.64)とコホート1のSMRは有意に高かった. 皮膚がんのSMRはコホート1が1.58 (0.24, 5.73)であったが, コホート2の観察死亡数がゼロであったため比較ができなかった. 著者らはこのコホート1, 2の推定線量の差（各々472 mSv, 132 mSv）は, コホート2に比べてコホート1でリンパ造血系のがんのリスクが高いことを説明するのに十分であると考えられると述べている.

2.2 米国

2.2.1 放射線科医

2.2.1.1 Matanoskiらによる研究[11)~13)]

(1) コホート

北米放射線学会(Radiological Society of North America)に1920–1969年の間に加入した放射線科医6,510人（全て男性）.

(2) 観察期間, 総観察人年

1920～1974年, 573,395人年.

(3) 平均線量

原著論文に記載なし.

(4) 結果

全人口を対照としたSMRを算出し, 比較のために被ばくの機会がほとんどない内科医, 耳鼻科医, 眼科医についても算出した. 放射線科医の全死亡, 全がん, 白血病のSMRは1.20, 1.31, 1.67であり, これは内科医の0.97, 0.98, 0.82, 耳鼻科医の0.96, 0.97, 1.04, 眼科医の0.83, 0.64, 0.57に比べて有意に高かった. また, コホートを従事開始年で1939年以前と1940年以降に分けて全死亡, 全がんの放射線科医の死亡率を他の専門医と比べた場合, 1939年以前では放射線科医の死亡率は他の専門医より高かったが, 1940年以降では50歳以前では低く, 50歳を過ぎると死亡率が上昇した. 著者らは, この結果の意味するところは明らかではないとしている.

2.2.1.2 Gonzálezらによる研究[14)]

(1) コホート

American Medical Association Physicians Masterfileに登録され, 米国において1902年以降に開業した放射線科医43,763人を対象とした. このうち女性は8,851人と20%を占める.

(2) 観察期間, 総観察人年

1979～2008年, 観察人年は原著論文に記載なし.

(3) 平均線量

原著論文に記載なし.

(4) 結果

放射線被ばくの機会がほとんどないと考えられる精神科医64,990人を対照群とし, SMR[(注2)]を算出した. 男性の全死亡のSMRは0.94 (95%CI: 0.90, 0.97)と有意に低かったが, Medical schoolの卒業年別に見た場合, 最近であるほど低い傾向が見られた. この傾向は全がん, 白血病, 皮膚がんでも見られ, 1939年以前に卒業した者のSMRは皮膚がんで6.38 (1.75, 23.20), 非ホジキンリンパ腫で2.69 (1.33, 5.45), 脳血管疾患で1.49 (1.11, 2.01)と有意に高く, これらの結果は放射線被ばくによる可能性があるとしている. しかし1960年以降に卒業した者では全がん, 皮膚がんのSMRの点推定値は1を下回っていた. 白血病における1939年以前に卒業した者のSMRは1.91 (0.83, 4.41)と点推定値はほぼ2であるが, 有意差はなかった. 女性は全死亡のSMRが0.83 (0.70, 0.97)と有意に低かったが, 部位別, 疾患別の解析では有意差がなかった.

2.2.2 放射線技師[15)~23)]

(1) コホート

米国では放射線技師の被ばく線量等がAmerican Registry of Radiologic Technologists (ARRT)というデータベースに登録されている. このデータベースに登録された者のうち, 米国のいずれかの州または地域に居住し, 1926～1982年の間にARRTに少なくとも2年間の認定を受けた放射線技師の記録から特定された146,022名をUS Radiologic Technologists (USRT)コホートとしている. このうち女性は73%と多数を占める.

(2) 観察期間, 総観察人年

1926～1997年[15)], 698,028人年[16)].

(3) 平均線量

観察期間を2008年まで延長した乳がんの解析では, 1960～1997年の線量記録を元に, 観察期間における乳房線量を37 mGyと推定した[17)]. ただしこれは上記(1)(2)のコホート, 観察期間のものとは（一部重複はあると思われるが）異なる.

(4) 結果

全死亡SMRは男性で0.76 (95%CI: 0.7, 0.8), 女性で0.76 (0.7, 0.8), 全がんSMRは男性で0.73 (0.7, 0.8), 女性で0.86 (0.8, 0.9)と有意に低かった[15)]. しかし罹患率で見た場合, 男性の固形がんSIRは0.92 (95%CI: 0.85, 0.98)と有意に低かったが, 女性では1.06 (1.02, 1.10)と有意に高かった[18)].

1960年以降に従事を開始した者を基準群とした死亡RR

[(注2)] 原著論文ではRR.

を従事開始年別に見た場合，全がん，乳がん，黒色腫では古い時期ほどRRが高い傾向が見られ，乳がんでは1940～1949年が2.44 (1.26, 4.75)，1939年以前が2.92 (1.22, 7.00)と有意に高かったが，1950～1959年に従事を開始した者では1.24 (0.77, 2.00)と有意差がなかった[15),19)]．乳がんを罹患率で見た場合も，1970年以降に従事を開始した者に対して，1934年以前に従事を開始した者のRRは2.9 (1.3, 6.2)と有意に高かったが，1950年以降の者では有意差がなかった[20)]．観察期間を2008年まで延長した解析では，罹患率，死亡率とも出生年が1929年以前の集団において有意に高い乳がんのERRが見られたが，出生年が1950年以降の集団では有意差がなかった．従事状況等から個人毎の乳房線量の推定を行った結果，1929年以前に従事を開始した集団における累積線量は1,168 mGyであり，1980年以降に従事を開始した集団では6 mGyであった[17)]．

その他の部位では，死亡率では脳の新生物で有意に高いHRが見られたが[21)]，肺がんでは見られなかった[22)]．罹患率では非黒色腫性の皮膚がんで，1959年以前に従事した集団において高いRRが見られた[23)]．

2.2.3　陸軍の放射線技師[24)]

(1) コホート

第2次世界大戦中に放射線技師として訓練された陸軍の放射線技師6,560人（全て男性）．

(2) 観察期間，総観察人年

1946～1974年，総観察人年は原著論文に記載なし．

(3) 平均線量

原著論文に記載なし．

(4) 結果

医療従事者，研究者，薬剤師を対照群として死亡率の比較を行った．がん，その他の死因において有意差は見られなかった．

2.3　英国：放射線科医[25)]

(1) コホート

英国のRadiological SocietyまたはRoyal College of Radiologistsに1897～1979年の間に登録された者2,698人（全て男性）．

(2) 観察期間，総観察人年

1897～1997年，69,615人年．

(3) 平均線量

原著論文に記載なし．

(4) 結果

登録時期を1897～1920年，1921～1935年，1936～1954年，1955～1979年の4群に分けた上で，男性開業医を対照群としたSMRを算出した．登録時期別の全がんのSMRは，各々1.75 ($p<0.001$)，1.24, 1.12, 0.71と古い時期ほど高い傾向が見られた．皮膚がんでは各々4.35, 4.55, 0.00, 0.00だが，前者の2つはいずれも観察死亡数が2例であり，後者の2つはゼロであるため比較はできない．

最初の登録からの経過年数別に見た場合，40年以上の群における全がんのSMRは1.41 (95%CI: 1.03, 1.90)と有意に高く，これは1954年以前に登録した者の寄与によると，著者らは述べている．がんを除いた全ての死因では登録時期が1897～1920年，1921～1935年のSMRがいずれも0.86と有意に低かったことから，著者らは，最初の登録から40年以上経過した期間におけるがん死亡率の高いSMRは，1921～1954年に最初の登録を行った群における放射線被ばくの長期的影響と考えられるとしている．また，被ばく線量が低かったと思われる1955年以降に最初に登録した放射線科医では，がん死亡率の増加を示す証拠はなく，がん以外の死因については，登録時期にかかわらずリスクが増加しているという証拠はなかったと述べている．

2.4　カナダ：放射線医療従事者[26)～28)]

(1) コホート

National Dose Registry of Canada（以下，NDR）に1951～1987年までに登録された者から，個人を特定する情報が不十分である者を除いた67,562人．内訳は内科医，看護師，放射線技師等であり，女性が65%を占める．

(2) 観察期間，総観察人年

1951～1987年，総観察人年は原著論文に記載なし．

(3) 平均線量

3.78 mSv．全員について線量が測定されている．

(4) 結果

カナダの一般国民を対照群としてSMR, SIRを算出した．全死亡のSMRは0.53 (90%CI: 0.51, 0.55)，全がんのSIRは0.78 (0.75, 0.82)と有意に低かった．女性の肝がんSIRが2.41 (1.05, 4.75)と有意に高かったが，症例数は6であり，著者らは偶然の可能性があるとしている．また，甲状腺がんのSIRは1.74 (1.40, 2.14)と有意に高かったが，NDRに含まれて，より高い外部被ばく量を受けた他の職業グループでは同様の増加が観察されなかった[23)]ことから，この結果は外部被ばくに関連しているとは考えにくく，少なくとも部分的には，医療へのアクセスが容易になった結果として説明できるとしている[27)]．

2.5　中国：X線作業者[29)]

(1) コホート

中国では放射線科医と放射線技師は厳密に区別されていないため，両者を含めたX線作業者を対象として，中国国内の24の地方にある大病院で1950年から1980年の間に雇用されたX線作業者27,011人をコホートとした．このうち女性は5,443人と20%を占める．また，コホートを1969年以前に雇用された者（コホート1：10,207人）と

1970年以降に雇用された者（コホート2：16,804人）に分割した．

(2) 観察期間，総観察人年

1950～1995年，694,886人年．

(3) 平均線量

職歴，従事状況等から，コホート1は551 mSv，コホート2は82 mSvと推定された．

(4) 結果

対照集団を同じ病院の外科医，内科医，耳鼻科医として，SIR [注3] を算出した．有意に高いSIRが全がん，白血病，固形がん，食道がん，肝がん，肺がん，膀胱がん，乳がん，皮膚がんで見られた．この有意に高いSIRは，乳がんを除いて男性従事者によってもたらされている．コホート1, 2のSIRは全がんで1.24, 1.08, 白血病では2.37, 1.73, 皮膚がんでは4.31, 2.74であり，いずれもコホート1のSIRは有意に高いが，コホート2のSIRは有意差がなかった．同様の傾向は固形がん，肝がん，膀胱がん，甲状腺がんでも見られたが，乳がんでは1.34, 1.33とほぼ等しい値となった．コホート1, 2の推定線量の違い（各々551 mSv, 82 mSv）から著者らは，電離放射線の長期分割照射によって累積線量が一定のレベルに達すると，有意ながんリスクが誘発されることを意味すると述べている．

2.6 デンマーク：放射線治療従事者[30]

(1) コホート

Finsen Institute, 及びAarhus Municipal Hospital に1954～1982年の間に従事し，1968年4月1日時点で生存している放射線治療従事者4,151人．内訳は看護師が42%，内科医が17%等となっており，女性が82%と多数を占める．

(2) 観察期間，総観察人年

1968～1985年，49,553人年．

(3) 平均線量

18.4 mSv．全員について線量が測定されている．

(4) 結果

全がんSIR [注4] は1.07 (95%CI: 0.91, 1.25) と有意差はなかった．前立腺がんでは6.02 (1.94, 14.06) と有意に高かったが，症例数が5例であるため，偶然の可能性が高いとしている．その他の部位では有意差は見られなかった．線量が測定された年数を1–2, 3–5, 6以上と区分し，各々についてSIRを見た場合，全がんでは1.04, 0.92, 1.21, 乳がんでは1.21, 1.26, 1.43と増加傾向が見られたが，有意差はなかった．著者らは，放射線量や被ばく年数とがんリスクとの間には関連性は認められなかったが，最初の被ばくからの時間が経過するにつれて，有意ではない弱い増加が認められた，と述べている．

2.7 その他

2.7.1 韓国[31]

Interventional radiology departmentsの従事者55人を対象とした研究では，LAR（Lifetime Attributable Risk：放射線被ばくに起因するがんの早期発症確率を10万人当たりの過剰症例数として算出した値）とLFR（Lifetime Fractional Risk：生涯ベースラインリスクに対するLARの比）を算出した．部位別に見た場合，最も高いLAR, LFRは甲状腺がんで見られた．

2.7.2 北欧[32]

デンマーク，フィンランド，アイスランド，ノルウェー，スウェーデンの国勢調査人口1,500万人と，追跡調査で得られた280万人のがん症例を元に，職業とがん罹患との知見を得るための生態学的研究 [注5] が実施された．著者らは白血病について，急性骨髄性白血病の環境および職業上の危険因子には，タバコの煙，（略），高線量放射線への曝露，高線量ベンゼンへの曝露，（略）などがあるが，今回の結果からは，これらの要因による影響を観察することは困難である，と述べている．

3. 原子力従事者

3.1 日本[33]

(1) コホート

1999年3月31日までに放射線業務従事者として（公財）放射線影響協会放射線従事者中央登録センターに登録された者のうち，1997年と2003年に実施した生活習慣等アンケート調査に回答し，喫煙について有効回答のある71,733人（全て男性）．コホートの大半を原子力発電施設の従事者が占め，その他は研究施設，燃料加工施設の従事者となっている．

(2) 観察期間，総観察人年

1999～2010年，591,000人年．

(3) 平均線量

25.5 mSv．全員について線量が測定されている．

(4) 結果

喫煙状況，総喫煙量，禁煙からの経過年数等を用いた喫煙調整により，ERR/Svが下がることが示された．喫煙調整前後のERR/Svは白血病を除く全がんが0.80 (90%CI: −0.39, 2.19) と0.29 (−0.81, 1.57)，肺がんが1.94 (−0.56, 5.26) と0.94 (−1.24, 3.90) であった．著者らは線量と喫煙との相関が示唆される場合には，喫煙が放射線リスクを評価する際の重要な交絡因子となると述べている．

[注3] 原著論文ではRR.
[注4] 原著論文ではRR.
[注5] 個人毎の情報を有する集団を用いるコホート研究と異なり，個人毎の情報を有しない集団（国，地域等）を単位として解析する研究方法．

3.2 米国

3.2.1 原子力発電施設等従事者[34]

(1) コホート

1979～1997年の間に15の原子力発電施設事業者（プラント数では52）に1年以上従事した53,698人．うち女性は6,387人で12%を占める．

(2) 観察期間，総観察人年

1979～1997年，698,051人年．

(3) 平均線量

25.7 mSv．全員について線量が測定されている．

(4) 結果

SMRは固形がんでは0.65 (95%CI: 0.59, 0.72)，非新生物疾患では0.34 (0.32, 0.36) と強い健康労働者効果が見られた．ERR/Svは固形がんが0.51 (−0.21, 4.64)，CLLを除く白血病が5.67 (−2.56, 30.4) と有意ではないが，非新生物疾患では6.40 (2.29, 12.2) と有意に高く，これは動脈硬化性心疾患の寄与が8.78 (2.10, 20.0) と大きいことによる．これについて著者らは，心臓疾患との関連性は他のいくつかの職業研究でも報告されているが，今回の関連性の大きさはそれらと一致していないため解釈には注意が必要であり，今後も注目していく必要がある，と述べている．

3.2.2 合同解析[35]

(1) コホート

過去に実施された軍事関連施設従事者や研究施設従事者の研究，即ちHanford[36),37)]，Idaho National Engineering and Environmental Laboratory[38)]，Oak Ridge National Laboratory[39)]，Portsmouth Naval nuclear shipyard[40)]，Savannah River[41),42)] の研究では，これらの施設に30日以上従事し，外部線量が記録された者をコホートとしている．合同解析ではこれらを統合した119,196人をコホートとした．うち女性は20%を占める．

(2) 観察期間，総観察人年

1944～1991年，4,019,065人年．

(3) 平均線量

20.2 mSv．全員について線量が測定されている．

(4) 結果

白血病を除く全がん，及びCLLを除く白血病のERR/Svは各々0.14 (95%CI: −0.17, 0.48)，1.7 (−0.22, 4.7) と有意ではなかったが，リンパ造血系のがんは2.0 (0.71, 3.5) と有意に高く，そのなかでもリンパ腫，多発性骨髄腫のERR/Svは各々，1.8 (0.027, 4.4)，3.9 (0.60, 9.6) と有意に高かった．著者らは，リンパ腫の高いリスク推定値は，本解析のコホートの一部であるSavannah River，英国，チェルノブイリ，その他医療被ばくを受けた者の研究で見られており，多発性骨髄腫の高いリスク推定値も，後述する15か国研究や英国の罹患率解析で見られていると述べている．

3.2.3 Million Worker Study[43)～45)]

(1) コホート

現在進行中の研究としてMillion Worker Study（以下，MWS．論文によってはMillion Person Studyと呼称されている．）がある．マンハッタン計画の期間中およびその後に雇用されたエネルギー省職員が36万人，原子力発電施設従事者が15万人，地上での核実験に参加した退役軍人が11.5万人，初期の放射線技師やその他の医療従事者が25万人，工業放射線技師が13万人となっており，総人数は現在のところ1,028,301人，うち女性は20%を占める．

(2) 観察期間，総観察人年

未発表．

(3) 平均線量

未発表．

(4) 結果

2019年時点での進捗状況は，30万人について完了（筆者（工藤）注：おそらく生死状況，死因，線量データ等の確定），残りについては3年以内に完了，あるいは調査開始予定とのことである．サブコホートについての解析結果は公表されているものもある[45)]が，MWSとしての解析は2022～2023年頃の完了が予定されている．

3.3 英国[46),47)]

(1) コホート

軍事関連施設，燃料加工・再処理施設，電力会社に1999年までに従事し，線量記録が保管されている167,003人．女性は16,437人と10%を占めている．

(2) 観察期間，総観察人年

1955～2011年，3,684,391人年．

(3) 平均線量

25.3 mSv（潜伏期10年を仮定した平均線量）．全員について線量が測定されている．

(4) 結果

白血病を除く全がんのERR/Svは死亡率で0.285 (90%CI: 0.06, 0.53)，罹患率で0.283 (0.10, 0.48) と有意に高かった．また，部位別がんにおいても死亡率では直腸，喉頭，膀胱，罹患率では直腸，胸膜，リンパ造血系等で有意に高いERR/Svが見られた．これらの結果について著者らは，長期の観察により狭い信頼区間を実現でき，得られたリスク推定値は原爆被爆者の研究結果と一致している，と述べている．

3.4 フランス[48)]

(1) コホート

使用済み燃料再処理，燃料加工等の燃料サイクル事業が主体のCEA-AREVA Nuclear Cycleにおいて1950～1994年の間に1年以上従事した者，または原子力発電施設が主

体のÉlectricité de Franceにおいて1961～1994年の間に1年以上従事した者について，1968年1月1日時点で生存し，線量が記録されていない者等を除外した59,004人．うち女性は7,436人で13%を占める．

(2) 観察期間，総観察人年

1968～2004年，1,469,949人年．

(3) 平均線量

18.4 mSv．全員について線量が測定されている．

(4) 結果

SMRは全死亡が0.60 (95%CI: 0.59, 0.62)，固形がんが0.68 (0.65, 0.71)と強い健康労働者効果が見られたが，胸膜がんでは1.69 (1.22, 2.27)，黒色腫では1.40 (1.02, 1.88)と有意に高かった．胸膜がんについては，従事年数が長いほどSMRが増加する傾向があったことから，著者らはアスベスト等の職業ばく露による可能性が部分的にあるかもしれないと述べている．しかしながら黒色腫については従事年数が長いほどSMRが減少する傾向となっており，そのような可能性は職業ばく露の可能性は支持されないとしている．

また，ERR/Svは固形がんが0.36 (90%CI: －0.42, 1.25)，CLLを除く白血病が3.52 (<0, 16.00)と有意ではないが，骨髄性白血病では14.95 (1.21, 43.61)と有意に高かった．骨髄性白血病の有意に高いERR/Svは最高線量群における1例の死亡によってもたらされており，また骨髄性白血病の原因となるベンゼンにばく露した可能性も考えられるため，解釈には注意が必要と著者らは述べている．

3.5 ロシア(Mayak)[49)～52)]

(1) コホート

1948年に核兵器製造施設として操業を開始したMayak Production Associationにおいて，1948～1982年の間に原子炉，放射科学施設，プルトニウム製造施設，水処理施設，機械修理施設に従事したことのある25,757人．うち女性は6,362人で25%を占める．

(2) 観察期間，総観察人年

1948～2015年，998,048人年．

(3) 平均線量

419 mGy（肺の外部線量）．ほぼ全員について線量が測定されているが，一部は職歴から推定された．

(4) 結果

ガンマ線による外部被ばくとプルトニウムによる内部被ばくの各々について肺がん死亡のERR/Gyを算出した．男性ではガンマ線0.164 (95%CI: 0.043, 0.300)，プルトニウム3.472 (1.534, 8.952)．女性ではガンマ線0.550 (－0.102, 1.274)，プルトニウム8.910 (2.671, 28.263)であった．これらの結果から著者らは，ガンマ線による外部被ばくとプルトニウムによる内部被ばくの両方で，肺がんの発生率が有意に増加したと述べている．また，肺，肝，骨を除いた固形がんでは0.12 (－0.73, 4.33)と有意に高いERR/Gyが見られており，喫煙経験の有無による喫煙調整はERR/Gyにほとんど影響を与えなかったとしている[50)]．CLLを除く白血病においても1.0 (0.5, 2.0)[51)]と有意に高いERR/Gyが見られている．

3.6 カナダ[53)～55)]

(1) コホート

Atomic Energy of Canada Limited (AECL), Ontario Hydro, Hydro-Quebec, New Brunswick Power Corporationにおいて1年以上従事した者をコホートとした．AECLは1949年に操業を開始したが，1956年の火災により線量記録が消失したため，コホートには1956年以降の従事者のみが含まれた．残りの3社の操業開始は1956年以降である．線量データの不備が判明したため[54), 55)]，修正に伴い若干名の除外，追加を行った45,316人を新コホートとして解析を行った．女性は7,619人と17%を占める．

(2) 観察期間，総観察人年

1956～1994年，613,648人年．

(3) 平均線量

21.64 mSv．全員について線量が測定されている．

(4) 結果

白血病を除く全がんのERR/Svは1.20 (95%CI: －0.73, 4.33)と有意ではなく，部位別がんでも有意に高い死因はなかった．

3.7 ドイツ[56)]

(1) コホート

旧西ドイツにある17の発電施設のいずれかにおいて，1991年1月1日時点で従事していた者，また，2008年12月31日までに従事を開始した者のうち，年間の実効線量が6 mSvを超える，または超える可能性がある従事を3か月以上継続した者8,972人．うち女性は226人と3%を占める．

(2) 観察期間，総観察人年

1991～2008年，130,737人年．

(3) 平均線量

29.5 mSv．全員について線量が測定されている．

(4) 結果

SMRは全死亡が0.50 (95%CI: 0.45, 0.56)，全がんが0.65 (0.51, 0.82)，非新生物疾患が0.43 (0.35, 0.53)と強い健康労働者効果を示し，有意に高い死因はなかった．HR/mSvは白血病を除く全がんが0.999 (95%CI: 0.996, 1.001)，肺がんが0.996 (0.990, 1.002)であり，有意に高い死因はなかった．

3.8 韓国

3.8.1 死亡率[57]

(1) コホート

1)医療，研究施設，2)その他の研究施設，教育施設，3)原子力発電施設，4)非破壊施設等，5)軍隊，公的組織等において，1984～2004年の間に電離放射線に被ばくした79,679人．うち女性は10,400人と13%を占める．

(2) 観察期間，総観察人年

1992～2004年，633,159人年．

(3) 平均線量

6.1 mSv．全員について線量が測定されている．

(4) 結果

一般国民を対照群としたSMRは全死亡が0.58 (95%CI: 0.54, 0.62)，全がんが0.73 (0.64, 0.82)と強い健康労働者効果を示し，有意に高い死因はなかった．ERR/Svは全死亡が1.7 (90%CI: −4, 7)，全がんが7.2 (−5, 21)であり，有意に高い死因はなかった．

3.8.2 罹患率[58]

(1) コホート

1978～2005年の間に4つの原子力発電施設において，線量計が支給された者のうち，1992年から2005年にかけて実施した生活習慣等のアンケート調査と健康診断に参加した者8,429人（全て男性）を放射線業務従事者とし，比較のために放射線被ばくのない7,807人も非放射線業務従事者として解析に含まれた．

(2) 観察期間，総観察人年

1992～2005年，63,503人年．

(3) 平均線量

19.9 mSv．全員について線量が測定されている．

(4) 結果

一般国民を対照群とした放射線業務従事者のSIRは全がんが1.07 (95%CI: 0.87, 1.30)と有意差はなかったが，甲状腺では5.93 (2.84, 10.9)と有意に高かった．甲状腺がんの有意に高いSIRについては，非放射線業務従事者のSIRも5.20 (2.24, 10.2)と有意に高いことから，広く実施されている検診の効果によると著者らは述べている．また，放射線業務従事者のERR/Svは白血病を除く全がんが2.06 (95%CI: −1.91, 9.0)，甲状腺が45.18 (<−12.13, 97.43)であり，有意に高い疾患，部位はなかった．

3.9 15か国研究[59)～61)]

(1) コホート

オーストラリア，ベルギー，カナダ，フィンランド，フランス，ハンガリー，日本，韓国，リトアニア，スロバキア，スペイン，スウェーデン，スイス，英国，米国による15か国のデータセットから，従事年数が1年以下の者等を除外した407,391人．うち女性は39,789人と10%を占める．

(2) 観察期間，総観察人年

1943～2000年，5,192,710人年．

(3) 平均線量

19.4 mSv．全員について線量が測定されている．

(4) 結果

日本，米国のIdaho National Laboratory，カナダのOntario Hydroのデータは社会経済状態のデータがないという理由で，これを調整する全がんや非がんの解析からは除外されたが，社会経済状態の調整を行わない白血病の解析には含まれた．白血病を除く全がんのERR/Gyは0.97 (90%CI: 0.27, 1.80)と有意に高かったが，CLLを除く白血病は1.93 (<0, 7.14)と有意ではなかった．白血病を除く全がんの有意に高いERR/Gyはカナダの寄与が大きく，カナダを除外した場合は0.58 (−0.10, 1.39)と有意ではなくなった．公表後にカナダの線量データに不備があり，これを修正した場合にはカナダ及び15か国解析のリスク推定値が下がることが判明した[54), 55)]．

3.10 INWORKS[62)～66)]

(1) コホート

米国，英国，フランスの3か国のコホートを合同した解析．米国101,428人(33%)，英国147,866人(48%)，フランス59,003人(19%)からなる総人数308,297人のコホートであり，各々3.2.2章，3.3章，3.4章で述べたコホートが基となっている．うち女性は40,035人と13%を占める．

(2) 観察期間，総観察人年

1944～2005年，8,221,032人年．

(3) 平均線量

20.9 mSv（結腸線量）．全員について線量が測定されている．

(4) 結果

白血病を除く全がんのERR/Gyは0.48 (90%CI: 0.20, 0.79)，CLLを除く白血病は2.96 (1.17, 5.21)，肺がんは0.56 (0.08, 1.02)と有意に高かった．また，非新生物疾患は0.19 (0.07, 0.30)，循環器系疾患は0.22 (0.08, 0.37)と有意に高かった．著者らはこれらの結果をもとに，低線量放射線と固形がん死亡率との関連について直接的な証拠が得られたとし，非新生物疾患についても放射線に影響される可能性があるとしている．

4. 考　　察

放射線科医，放射線技師をコホートとした研究では，古い時代（概ね1950年以前）から観察を開始している研究も幾つかある[15)～25), 29)]．しかし概してコホートの人数が多くないため，総観察人年が50万を超えているのは米国の放射線科医，放射線技師[15)～23)]と中国のX線技師[29)]の研究のみである．カナダ[26), 27)]，デンマーク[30)]の研究ではコホート全員の線量が記録されていたが，古い時代では個人

毎の線量データがないものが多く，日本の放射線技師[8]，米国の放射線技師[17]，中国のX線技師[29]の研究では従事状況等から線量が推定されているが，他の研究では行われていない．おそらくこのような事情を反映して，放射線科医，放射線技師をコホートとした研究では暦年間で死亡率（または罹患率）を比較する手法が多く用いられている．この結果，古い時代において全がんが高リスクを示す傾向が見られた．これを疾患別に見た場合，白血病，皮膚がん，乳がんにおいて同様の傾向が見られた．一方，近年の従事者では高リスクは見られていない．放射線科医の年間の平均被ばく線量は，1920～1929年では900～7,000 mSv，1930～1949年では50～100 mSvであったが，法規制，線量低減技術の進歩等により1950年代前半では50 mSv，1960年代前半では5 mSvと大きく下がった．以降1970年代から10年ごとに1 mSv, 0.75～0.34 mSv, 0.55～0.12 mSvとなり，2000年以降では0.23～0.08 mSvと推定されている[67]．幾つかの疾患が古い時代において高リスクを示し，近年で見られていないことは，被ばく線量の違いによる可能性が考えられる．一方，このことは，近年の従事者は相対的に若く，がんの好発年齢に十分達していないことによる可能性も考えられるため，より長い観察が望まれる．

米国の放射線技師[15)~23)]，カナダ[26),27)]，デンマーク[30)]の研究ではコホートの半数以上を女性が占め，女性に関する健康影響の知見を得られている点で，貴重な研究と言える．米国の放射線技師（USRTコホート）については線量も推定され，解析結果がコンスタントに発表されており，今後の解析が待たれる．

放射線科医，放射線技師は国家資格であり，一般に学歴は高く，健康的な生活習慣を送っていると考えられる．このため，これらのコホートでは被ばく線量の多寡によって，生活習慣，社会経済状態等の特性が大きく異なることは考えにくい．一方，原子力従事者のコホートは，一つのコホート内に電力会社，研究機関，燃料加工，非破壊検査，核兵器製造等，様々な職種が混在していることがあり，コホート内の異質性は放射線科医，放射線技師より大きいと考えられる．このため，原子力従事者のコホートは，放射線科医，放射線技師のコホートに比べて生活習慣，社会経済状態が交絡因子となっている可能性が高いと考えられる．

原子力産業が本格化したのは，放射線の医療利用より新しい時代であるため，原子力従事者の研究における観察開始は古いものでも1940年代からと放射線科医，放射線技師の研究より新しい時期となっている．しかしコホートの人数は概して放射線科医，放射線技師より大きいため，総観察人年が100万を超えている研究もある[35),46),48),59)~66)]，被ばく線量は放射線科医，放射線技師より低く，ロシアのMayakを除いて概ね20 mSv前後となっている．

原子力従事者の解析結果は一貫していない．白血病を除く全がん（または全がん，固形がん）において有意に高いERR/Sv(ERR/Gy)を示した結果[46),50),59),62)]がある一方で，有意差がない結果[33)~35),48),53),56)~58)]もある．

日本の原子力従事者を対象とした研究[33)]における喫煙状況，総喫煙量，禁煙からの経過年数を用いた喫煙調整が放射線リスク推定値を下げ，死因によっては半分程度となるという結果は，原子力従事者コホートを用いて放射線リスクを検討する際の，交絡因子調整の重要性を示している．

Mayak[49)~52)]のコホートはガンマ線による高い外部線量と共に，プルトニウムによる高い内部被ばく線量を有している点で特異的である．肺，肝，骨を除く固形がんの解析[50)]では，喫煙調整はERR/Gyにほとんど影響を与えなかったとしている．これは喫煙感受性の高い肺，肝を除外したことによる可能性もあるが，一方で，喫煙情報が喫煙経験の有無だけであり，総喫煙量等を考慮していないことによる可能性も考えられる．肺がんの解析[49)]では総喫煙量，プルトニウム線量の調整により，外部線量によるERR/Gyが0.64 (95%CI: 0.45, 0.84)から0.19 (0.07, 0.31)に下がることが示されている．ただし総喫煙量の算出に当たって，喫煙データを有しない女性従事者は全て非喫煙としたことや，喫煙本数と喫煙開始年齢が得られなかった従事者（喫煙者の43%）について平均値を代入したことには，不確かさがあるように思われ，この点は著者らも研究の限界と述べている．

現在，原子力従事者をコホートとした研究で最も注目されている研究はINWORKS[62)~66)]であろう．INWORKSの参加国である米国，英国，フランスを個別に解析した場合の，白血病を除く全がんのERR/Svは米国が0.14，英国が0.28，フランスが0.34であるが，この3か国を合同したINWORKSのERR/Gyは0.48となっており，各国個別のERR/Sv (0.14～0.34)より高くなっている．この原因は，INWORKSが各国個別の解析とは異なる手法を採用したこと，即ち，(1)結腸線量を使用したこと，(2)従事期間が1年未満の者を除外したこと（フランスは個別の解析でも，この規準を採用），(3)中性子モニタリング状況を調整したこと，に起因する可能性が指摘されている[68)]．

既に述べたように，原子力従事者の解析結果は一貫していない．この原因の一つは，交絡因子の調整等の解析手法が研究間で異なることに起因する可能性も考えられる[69)]．放射線疫学の結果の解釈に当たっては，この点にも留意する必要があると思われる．

付記

本稿の3.1章で取り上げた日本の原子力従事者の研究は原子力規制委員会原子力規制庁の委託業務として実施したものである．開示すべき利益相反はない．

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PAPER

Reanalysis of cancer mortality using reconstructed organ-absorbed dose: J-EPISODE 1991–2010

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Abstract

The Japanese Epidemiological Study on Low-Dose Radiation Effects (J-EPISODE) has been conducted since 1990 by the Radiation Effects Association to analyse health effects for nuclear workers. It uses the recorded doses, i.e. dosimeter readings, evaluated in $H_p(10)$ for estimation of radiation risk; however, the International Commission on Radiological Protection does not recommend the use of effective doses for epidemiological evaluation and instead recommends the use of organ-absorbed doses for assessing cancer risk. Recently, the J-EPISODE has developed a conversion factor that can convert dosimeter readings to organ-absorbed doses following, in principle, the approach adopted by the International Agency for Research on Cancer 15-Country Collaborative Study. The approach was modified based on recent dosimeter usage practices and the Japanese physique. The aim of this study was to reanalyse the excess relative risk (ERR) of cancer mortality for the J-EPISODE using the previous analysis method but substituting the organ-absorbed dose for the recorded dose to confirm the adaptability and relevance of organ-absorbed doses for the J-EPISODE. The organ-absorbed doses from 1957 to 2010 were reconstructed for the whole cohort. The cancer mortality risk was reanalysed with Poisson regression methods, first by comparing the ERR/Gy for all cancers excluding leukaemia with the risk after excluding lung cancer for the whole cohort of 204 103 participants. In the whole cohort, all cancers excluding leukaemia, lung cancer and non-Hodgkin's lymphoma had statistically significant positive ERR/Gy estimates; leukaemia excluding chronic lymphocytic leukaemia had negative but not statistically significant estimates. Gallbladder cancer and pancreatic cancer showed statistically significant negative. Then, a subcohort of 71 733 respondents was selected based on lifestyle surveys with data on qualitative smoking status as well as quantitative smoking information on pack-years. Pack-years for current smokers and former smokers and years since the cessation of smoking for former smokers were used for the smoking-adjusted model. The most important feature of the J-EPISODE revealed to date was a decreasing tendency of the ERR/Sv by the smoking adjustment. For almost all causes of death such as lung cancer and stomach cancer, the estimated ERR/Gy decreased by the smoking adjustment, although those for the colon, prostate and kidney and other urinary organs were almost the same after the adjustment. This tendency remained unchanged even when using the organ-absorbed dose, indicating the appropriateness of using organ-absorbed doses for further risk analysis. At the same time, it indicated that confounding by smoking seriously biased the radiation risk estimates in the J-EPISODE and thus should be accounted even if organ dose is used.

1. Introduction

1.1. Construction of conversion factors from dosimeter readings to organ-absorbed doses

Since 1990, the Institute of Radiation Epidemiology of the Radiation Effects Association (REA) has been conducting a nuclear worker cohort study, the Japanese Epidemiological Study on Low-Dose Radiation

Effects (J-EPISODE), to analyse the health effects. The J-EPISODE has estimated the radiation risk associated with photon exposure assessed in the personal dose equivalent, $H_p(10)$, which is a good estimator of the effective dose. The Japanese nuclear industry started in the late 1950s, and the annual recorded doses, i.e. dosimeter readings, from 1957 to 2010 evaluated in $H_p(10)$ were provided by the Radiation Dose Registration Center (RADREC), REA (Asano and Ito 2019). The endpoints were cancer deaths until the present. Cancer incidence data have also been available since 2016 from the National Cancer Registry (Matsuda and Sobue 2015).

The J-EPISODE has recently constructed organ-absorbed dose conversion coefficients from dosimeter readings recorded in RADREC, as described in the sister papers (Furuta *et al* 2020a, 2020b, 2021). Although the concept of effective dose and its operational definition of personal dose equivalent are widely used for radiological protection purpose, the International Commission on Radiological Protection (ICRP) does not recommend the use of effective doses for epidemiological evaluation (ICRP 2007); rather, it recommends using organ-absorbed doses for cancer risk evaluations in epidemiological cohort studies. The method adopted by the J-EPISODE was based on established organ dose reconstruction methods and followed, in principle, the methodology of the International Agency for Research on Cancer (IARC) 15-Country Collaborative Study (hereinafter called the 15-Country Study) (Thierry-Chef *et al* 2007). The framework for the conversion from a dosimeter reading to an organ-absorbed dose was summarised as follows:

(a) The 15-Country Study examined the dosimeter response to photon exposure for the dosimeter types of old film badges (FBs), multi-element FBs and thermoluminescence dosimeters (TLDs). Data for the dosimeter types recently in use were supplemented with data obtained by the J-EPISODE from experiments on the dosimeter response—dosimeter reading per air kerma—for radio-photoluminescent glass dosimeters (glass badges [GBs]), active personal dosimeters (hereinafter called electronic personal dosimeters [EPDs]) and optically stimulated luminescence dosimeters (Luminess badges [LBs]). The supplementary data were obtained using a device that irradiated an anthropomorphic phantom in the Japan Atomic Energy Agency (JAEA) calibration laboratories.

(b) The reconstruction of an organ-absorbed dose required information on the photon energy and geometry distribution of the exposed population. The J-EPISODE employed the 15-Country Study assumption; on average, in nuclear power plants (NPPs), 10% of the dose received by nuclear workers was due to photon energies ranging from 100 to 300 keV and 90% from photon energies ranging from 300 to 3000 keV. In mixed activities (MA) facilities, such as research and development organisations and fuel processing factories, 20% of the dose came from photon energies ranging from 100 to 300 keV and 80% from photon energies ranging from 300 to 3000 keV, with the average geometry being 50% in the anteroposterior geometry and 50% in the isotropic geometry for NPPs and MA facilities. A literature survey also disclosed survey reports jointly conducted by Japanese electric power companies in the 1980s. The analysis of the working environments of Japanese workers in NPPs demonstrated the appropriateness of applying the 15-Country Study assumption for nuclear workers in Japan.

(c) The J-EPISODE subjects differ physically from the references defined by the ICRP. The 15-Country Study used a conversion coefficient computed from ICRP Publication 74, which was a simulation result using the reference computational phantom for an adult male based on the standard Caucasian physique (ICRP 1996). By contrast, the J-EPISODE estimated a conversion coefficient from air kerma to an organ-absorbed dose based on JM-103—an adult male voxel phantom with an average Japanese size (Sato and Takahashi 2012). Eventually, the differences in conversion coefficients were small. The conversion coefficient was estimated for the following 14 tissues/organs: the colon, red bone marrow (RBM), oesophagus, stomach, liver, gallbladder, spleen, lungs, pancreas, prostate, bladder, kidneys, brain and heart.

(d) Bias regarding any differences in dosimeter calibration was taken into account, because until 1988, the physical quantity of exposure—expressed in terms of roentgen (R) units—was measured by personal dosimeters calibrated in free air. By contrast, personal dosimeters since 1989 have been designed to measure phantom-related operational quantities. Therefore, the bias factor for the recorded doses in Sv until 1988 was defined as the ratio between the recorded dose $H_p(10)$ raised by backscatter radiation from the body and the delivered dose in $H_p(10)$.

(e) Integration of the above-mentioned factors using a mathematical model of a lognormal distribution resulted in the conversion factors from the dosimeter reading to the organ-absorbed dose by dosimeter type (FB, TLD, GB, EPD and LB), nuclear facility type (NPP or MA facility) and period (until 1988 or since 1989). Figure 1 shows the conversion factor, the organ-absorbed dose per dosimeter reading (Gy/Sv), according to tissue/organ for selected combinations of dosimeter types, nuclear facility type and period. The conversion factor was approximately 0.7–0.9 Gy Sv^{-1} (Furuta *et al* 2021). The values were higher in the lungs, stomach and gallbladder but lower in the kidneys, prostate and spleen. According to dosimeter type, the dosimeter responses for FB and LB contributed less than those for EPD, GB and TLD. The contribution of

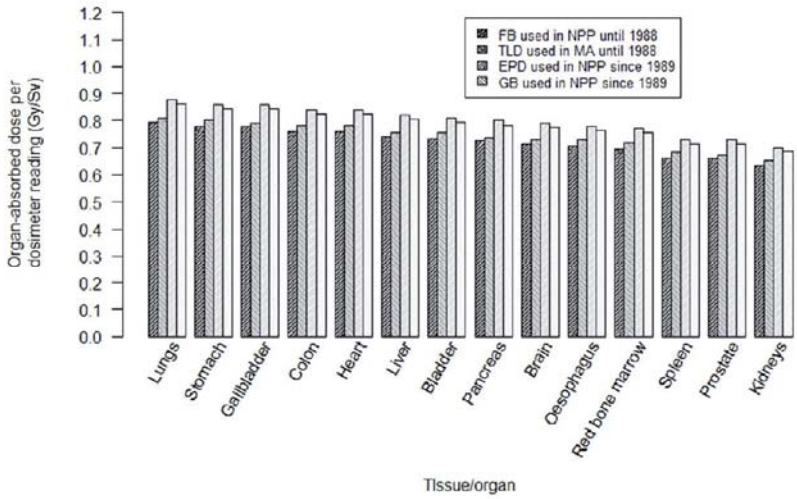

Figure 1. Conversion factor from the dosimeter reading to the organ-absorbed dose (Gy/Sv) by tissue/organ for specific combinations of dosimeter type, nuclear facility type and period; Film badge (FB) used in NPPs until 1988, TLD used in the mixed activities (MA) facilities until 1988, EPD used in NPPs since 1989 and Glass badge (GB) used in NPPs since 1989.

the dosimeters from MA facilities was approximately 2% less than that of dosimeters from NPP facilities. In the period until 1988, the roentgen era, the contribution was approximately 4% lower than that in the period since 1989 (Furuta *et al* 2021).

For more details about the methods used to estimate organ-absorbed doses, please refer to the sister papers (Furuta *et al* 2020a, 2020b, 2021).

1.2. Smoking as a possible confounding factor

One advantage of the J-EPISODE was that it has information on smoking and the earlier analyses suggested that smoking might be a strong confounder in the association between radiation and cancer mortality. The REA (2015) compared the estimated excess relative risks (ERRs)/Sv for all cancers excluding leukaemia for all 204 103 participants, and for all cancers excluding lung cancer and excluding leukaemia. The REA (2015) also compared the 75 442 respondents to lifestyle surveys who reported smoking information, for their estimated ERRs/Sv for all cancers excluding leukaemia, with and without the smoking adjustment, using qualitative information on smoking status. Of the 75 442 participants, 71 733 had quantitative information on pack-years. These data were analysed and the estimated ERRs/Sv for all cancers excluding leukaemia with and without the smoking adjustment were compared. Details were described in Kudo *et al* (2018).

1.3. Previous nuclear worker cohort studies on cancer risk: pros and cons

The Life Span Study (LSS) of Atomic bomb survivors is regarded as the gold standard for radiation protection from high-dose and high-dose-rate radiation exposures (Ozasa *et al* 2012, Grant *et al* 2017). Many cohort studies have been conducted on nuclear workers to investigate the effects of low-dose and low-dose-rate radiation exposures, but the results remain controversial. The goal of many occupational cohort studies on nuclear workers was to obtain risk estimates, compatible with that of the LSS, for low-dose/low-dose-rate radiation effects directly from the cohort instead of extrapolating from the results of the LSS for high-dose/high-dose-rate exposures. Therefore, accumulation of a large number of person-years of follow-up and observed deaths is crucial to obtain precise risk estimates for prolonged low-dose and low-dose-rate exposures. Of these studies, historical cohort studies, such as the 15-Country Study (Cardis *et al* 2007, Vrijheid *et al* 2007) and the International Nuclear Workers Study (INWORKS) (Richardson *et al* 2015, Hamra *et al* 2016), which set their retrospective observations from the 1940s or 1950s, already fulfilled this requirement. The long follow-up duration was a strength and contributed to the improved accuracy of

the risk estimates. One of the features of occupational exposure cohorts is that each worker carries a personal dosimeter; thus dose information on external exposure, which is the dominant dose, can be obtained relatively accurately. However, the uncertainty regarding dosimetry in the early years and especially the possible exposure to neutrons in relation to nuclear weapons production are also weaknesses of the cohorts (Fix *et al* 1997, Wakeford 2021). The study of dose errors remarkably progressed during the 15-Country Study and organ doses were reconstructed. Another weakness was the lack of control of potential confounders.

In contrast to the historical cohort studies, the J-EPISODE mostly consisted of NPP workers and started its follow-up in the 1990s using the doses recorded since 1957. It has to accumulate person-years to obtain reliable results. The J-EPISODE did not experience such serious problems with dosimetry as those in the historical cohort studies because the nuclear industry started later in Japan than in the United States and Western Europe, and the J-EPISODE did not include nuclear weapons industries. The J-EPISODE finally performed an organ dose reconstruction and is now in the same position as the historical cohort studies with regard to dosimetry. Its weakness was its short follow-up period, which resulted in unstable risk estimates with wide confidence intervals (CIs). However, the limited uncertainty regarding dosimetry and the possible control of confounders were its advantages.

1.4. Aim

The primary aim of this study was to reanalyse the ERR of cancer mortality for the J-EPISODE using the same method used in previous analyses, except the reconstructed organ-absorbed dose was used instead of the recorded dose. The second aim was to confirm the adaptability of organ-absorbed dose and relevancy of the estimated radiation risk obtained by using organ-absorbed dose for the J-EPISODE.

2. Methods

The manuscript focused on determining whether the main features of the results remained unchanged regardless of whether the doses applied for the analysis were the recorded doses or the reconstructed organ-absorbed doses. The analysis methods for risk estimation for the J-EPISODE have been described elsewhere (REA 2015, Kudo *et al* 2018). Here, we briefly describe the method in terms of the comparability between the present study and the previous studies.

2.1. Cohort definition

Two cohorts were included in the analysis: the whole cohort and the subcohort. The whole cohort consisted of 204 103 Japanese male workers who were registered with the RADREC as of the end of March 1999. The whole cohort was followed up from 1991 to 2010. The subcohort consisted of 71 733 participants from the whole cohort who responded to the lifestyle surveys described below and who included smoking information on pack-years (hereinafter referred as the subcohort). The subcohort was followed up from 1999 to 2010 (table 1).

2.2. Dosimetry

The Japanese nuclear industry started in the late 1950s. Doses received by each worker in the controlled areas were monitored with a personal dosimeter. The doses were evaluated in mSv of $H_p(10)$ and conceptually consisted of external and internal exposure doses. However, the doses received were assumed to be derived predominantly from the photon in the energy from 100 keV to 3 MeV. Each nuclear facility periodically submits its records of individual annual doses to the RADREC. These records include doses received by the own employees and contractors' workers. The J-EPISODE was provided by the RADREC with the annual recorded doses from 1957 to 2010 for each worker and each facility.

2.2.1. Organ dose reconstruction

A specific organ-absorbed dose was reconstructed based on each worker's annual recorded dose from each nuclear facility in each year categorised into an NPP or MA facility and a specific dosimeter type assigned as the primary personal dosimeter in the facility. The specific organ-absorbed dose for each worker in each year was obtained by multiplying the categorised individual annual recorded dose in Sv by the corresponding conversion factor (Gy Sv) and then summing them for each worker and year (Furuta *et al* 2021).

2.3. Follow-up of vital status and underlying causes of death

The endpoint of the J-EPISODE was cancer death to date. The vital status of each participant was verified by applying to the municipality for the issuance of his Resident Registration Card (RRC). If the participant was

Table 1. Profile of the J-EPISODE.

Item	The whole cohort	The subcohort with smoking information on pack-years	ICD-10 codes
Cohort size for analysis	204 103 males	71 733 males	
Follow-up period	1991–2010	1999–2010	
Total person-years	2889 000	591 000	
Mean years of follow-up	14.2	8.2	
Number of deaths			
All cancers (ca) excluding leukaemia	7929	1326	C00–C97 except C91–C95
Ca of oral cavity and pharynx	201	37	C00–C14
Oesophageal ca	441	87	C15
Stomach ca	1407	218	C16
Colon ca	535	100	C18
Rectum ca	398	68	C19–C21
Liver ca	1219	138	C22
Gallbladder ca	261	38	C23–C24
Pancreatic ca	531	109	C25
Lung ca	1756	319	C33–C34
Prostate ca	192	39	C61
Bladder ca	103	14	C67
Ca of kidney and other urinary organs	145	20	C64–C66, C68
Non-Hodgkin's Lymphoma	176	34	C82–C85, C96
Multiple myeloma	60	14	C88, C90
Leukaemia excluding chronic lymphocytic leukaemia	207	44	C91–C95 except C91.1
Mean cumulative colon absorbed dose since 1957 at the end of follow-up (mGy)	11.0	20.1	
Mean age (years)	55.6 at the end of follow-up	45.1 at the date of survey response	

still alive, a copy of his RRC was issued; if he was deceased or had moved, a record deleting his RRC was issued. A new application for issuance was made at the new addresses of participants who had moved. The maximum retention period for the deleted records at the municipality was five years until 2020, but it has since been extended to 150 years. Therefore, RRC inquiries to municipalities were conducted at intervals of less than five years.

For participants whose deaths were ascertained through RRCs, the underlying causes of death were obtained by record linkages with the death records of the Vital Statistics approved for use and provided by the Ministry of Health, Labour and Welfare. Underlying causes of death in the death certificates were coded according to the International Classification of Diseases (ICD) tenth revision (Iwasaki *et al* 2000).

2.4. Lifestyle surveys

The J-EPISODE conducted lifestyle surveys in 1997 and 2003 among different samples of the whole cohort to obtain the potential confounding factors. The number of respondents was 46 141 for the first survey and 41 742 for the second survey. Some participants responded to both surveys, but only the first survey responses were analysed in the present study. The first survey examined the participants' characteristics, such as occupational history and lifestyle, which included questions on smoking status (current, former and never), age at starting to smoke, number of cigarettes smoked per day and age of the cessation of smoking for former smokers. In addition to these questions, the second survey questionnaire included information on educational history and jobs at nuclear facilities (Murata *et al* 2002).

Here, figure 2 illustrates the variables z_1 and z_2 for the pack-years, which were calculated as the number of smoking years multiplied by the number of cigarettes per day and divided by 20 (cigarettes per pack). For current smokers, z_1 was the number of smoking years since the age at starting to smoke through the age at the survey date. For former smokers, z_2 used the number of smoking years since the age at starting to smoke until the age of the cessation of smoking, and the variable z_3 was calculated as the non-smoking years since the cessation of smoking until the age at the survey date. For participants who had never smoked, z_1–z_3 were zero.

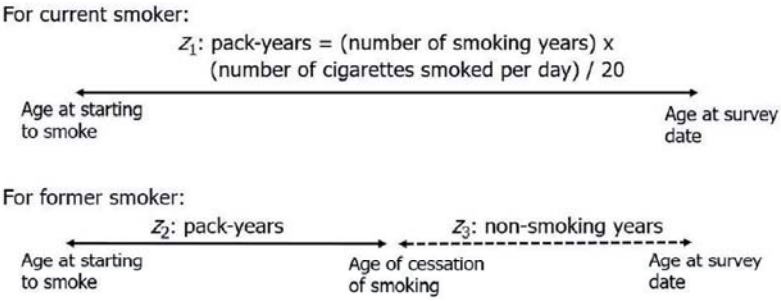

Figure 2. Illustration of pack-years for current and former smokers.

2.5. Risk estimation models

The ERR for mortality from all cancers excluding leukaemia among the male Japanese nuclear workers was estimated using a linear model and a Poisson regression method, which was applied for cross-classified data of the number of deaths and person-years. Dose accumulation lagged by two years for leukaemia excluding chronic lymphocytic leukaemia (CLL) and 10 years for other cancers. For each cancer from a tissue/organ, the corresponding organ-absorbed dose was primarily applied for the analysis. Where this was not applicable, the colon absorbed dose was applied not only for rectum cancer but also for all cancers excluding leukaemia. The RBM absorbed dose was applied for non-Hodgkin's lymphoma, multiple myeloma and leukaemia excluding CLL. The oesophagus absorbed dose was applied for cancers of the oral cavity and pharynx, and the stomach absorbed dose was applied for pancreatic cancer.

2.5.1. Model for the whole cohort

For the whole cohort of 204 103 male participants, the following model was applied:

$$\lambda = \lambda_0(a, c, r)(1 + \beta d), \tag{1}$$

where λ was the mortality rate at the cumulative organ-absorbed dose d (Gy), λ_0 was the background mortality rate stratified by a, c and r; a was the attained age (20–, 25–, …, 95– and 100+), c was the calendar year (1991–1994, 1995–1999, 2000–2004 and 2005–2010) and r was the residence area (Hokkaido + Tohoku, Kanto, Hokuriku, Chubu, Kinki, Chugoku, Shikoku and Kyushu + Okinawa); β was the parameter of the ERR/Gy; d was categorised into six groups by mGy levels of <5, 5–, 10–, 20–, 50– and 100+. This model was identical to that used in the previous analysis by the REA (2015), except for the use of the organ-absorbed dose instead of the recorded dose. Comparisons were first made between the ERRs/Gy from the present study and the ERRs/Sv from the previous study. Comparisons were then made between the ERR/Gy for all cancers excluding leukaemia and the ERR/Gy for all cancers excluding lung cancer and excluding leukaemia.

2.5.2. Model for the subcohort

For the subcohort of 71 733 participants who had smoking information on pack-years, the following model was applied for the smoking adjustment:

$$\lambda = \lambda_0(a, c, y, r, s)\exp(\alpha_1 z_1 + \alpha_2 z_2 + \alpha_3 z_3)(1 + \beta d), \tag{2}$$

where λ was the mortality rate at the cumulative organ-absorbed dose d (Gy), λ_0 was the background mortality rate stratified by a (attained age; the same category as (1)), c (calendar year; <2000, 2000–2004 and 2005–2010), y (birth year; <1920, 1920–, 1925–, …, and 1970+), r (residence area; the same as (1)) and s (survey indicator; the first or the second). β was the parameter of the ERR/Gy. d was categorised into 14 groups by mGy levels: 0, >0, 1–, 2–, 3–, 5–, 7.5–, 10–, 15–, 20–, 25–, 50–, 100– and 200+. In the exponential term, the variables z_1–z_3 defined in section 2.4 were employed and α_1–α_3 represented the respective coefficients of z_1–z_3. Pack-years of z_1 and z_2 were categorised into eight groups: 0, >0, 10–, 15–, 20–, 25–, 30– and 50+. The non-smoking years of z_3 since the cessation of smoking were categorised into three groups;

Table 2. Cumulative dose of $H_p(10)$ and a specific organ-absorbed dose during 1957–2010 for the whole cohort of 204 103 participants in the J-EPISODE.

		Organ-absorbed dose (mGy)		
	Recorded dose $H_p(10)$ (mSv)	Colon	Lungs	Red bone marrow
Mean cumulative dose since 1957 at the end of follow-up	13.9	11.0	11.5	10.1

<5, 5– and 10+. This model was identical to the previous analysis by Kudo *et al* (2018) except for the use of the organ-absorbed dose instead of the recorded dose.

The ERR/Gy, except for the smoking confounder, was directly and quantitatively estimated by the smoking-adjusted model (2) with the exponential terms of pack-years variables. Therefore, the effect of smoking as a confounder was determined by comparing the ERRs/Gy between the smoking-adjusted model (2) and the non-adjusted model without the exponential term: $\lambda = \lambda_0 (a, c, y, r, s)(1 + \beta d)$.

The relative risk (RR) of pack-years of smoking by pack-year category was estimated by modifying model (2). The numerical variables z_1 and z_2 in model (2) were categorised; a pack-year categorical variable z_4 including current smoker, former smoker as well as non-smoker was generated; then $\exp(\alpha_1 z_1 + \alpha_2 z_2 + \alpha_3 z_3)$ in model (2) were replaced with $\exp(\gamma_1 z_4 + \gamma_2 z_3)$. The RR was obtained as the exponential of the estimated γ_1.

3. Results

3.1. Reconstructed organ-absorbed dose for the J-EPISODE from 1957 to 2010

Table 2 shows the comparison of the cumulative dose between the recorded dose in $H_p(10)$ and a specific organ-absorbed dose reconstructed in the present study. The mean cumulative dose in $H_p(10)$ was 13.9 mSv in 2010, and the mean cumulative organ-absorbed dose was 11.0 mGy for the colon, 11.5 mGy for the lungs and 10.1 mGy for RBM. Neglecting dose unit differences, the organ dose values were approximately 0.8 times the recorded doses. This indicated that the recorded doses were overestimated in terms of the organ-absorbed dose.

3.2. Reanalysis results for the whole cohort

The whole cohort consisting of 204 103 participants with follow-up from 1991 to 2010 had a total person-years number of 2.9 million, a number of observed deaths from all cancers excluding leukaemia of $n = 7929$ and a mean age at the end of follow-up of 55.6 (table 1). As for the number of deaths by cancer site, lung cancer ($n = 1756$), stomach cancer ($n = 1407$) and liver cancer ($n = 1219$) contributed 55%. Figure 3 and table 3 shows the ERRs/Gy by causes of death using the organ-absorbed dose for 204 103 participants with follow-up in 1991–2010 in comparison with the ERRs/Sv using the recorded dose in $H_p(10)$. For all cancers excluding leukaemia, the estimated ERR/Gy and 90% CI was 1.22 (0.24, 2.26), which were statistically significant positive but possibly confounded by smoking, because it decreased to 0.50 (−0.56, 1.56) when excluding lung cancer. The CIs for site-specific cancers were wider due to the small number of observed deaths (figure 3). Statistically significant positive estimates of ERR/Gy were only observed for the lung (4.00 [1.81, 6.49]), with $n = 1756$ and for non-Hodgkin's lymphoma (11.35 [2.58, 23.70]), with $n = 176$, in addition to all cancers excluding leukaemia. Positive but not statistically significant estimates were seen for the eight site-specific cancers. Statistically significant negative estimates were observed for the gallbladder (−4.87 [−7.05, −1.15]), with $n - 261$, and for the pancreas (−5.29 [−7.21, −2.54]), with $n = 531$. In addition to the estimates for leukaemia excluding CLL (−0.42 [−5.38, 7.59]) with $n = 207$, other two cancers were observed negative but not statistically significant.

3.3. Reanalysis results for the subcohort

The subcohort consisting of 71 733 participants with follow-up in 1999–2010 had a number of total person-years of 0.6 million, a number of observed deaths from all cancers excluding leukaemia of $n = 1326$ and a mean age at the date of survey response of 45.1 (table 1). Figure 4 and table 4 shows the ERRs/Gy and 90% CIs by causes of death with the smoking adjustment using pack-years for the subcohort and a comparison with the ERRs/Gy without the smoking adjustment. The estimated ERR/Gy for all cancers excluding leukaemia decreased from a ERR/Gy of 1.00 (−0.55, 2.82) without the smoking adjustment to 0.25 (−1.16, 1.92) with the smoking adjustment. For leukaemia excluding CLL—this is also an important tissue for radiation protection—the estimate of the ERR/Gy did not converged due to a small number of deaths ($n = 44$). By cancer site, the ERR/Gy decreased from 3.09 (−0.11, 7.34) to 1.56 (−1.15, 5.25) for lung cancer

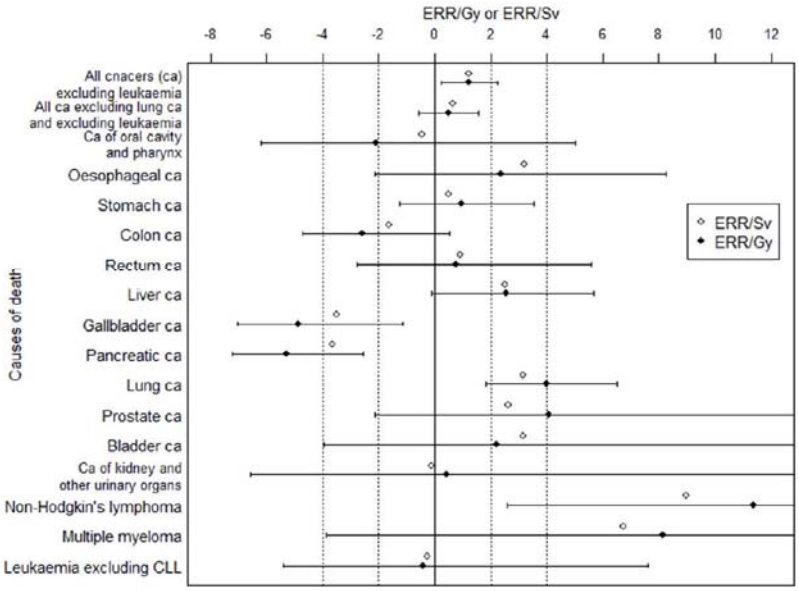

Figure 3. ERR/Gy and 90% CI by causes of death using the organ-absorbed dose for the whole cohort of 204 103 participants in the J-EPISODE with follow-up in 1991–2010 in comparison with ERR/Sv using $H_p(10)$.
Note: (1) The ERRs/Gy were estimated using the organ-absorbed dose, while the ERRs/Sv were estimated using the recorded dose in $H_p(10)$.
(2) The 90% CIs of the ERRs/Gy were based on the likelihood method. The lower bounds of the CIs for the oral cavity and pharynx, gallbladder, pancreas, and kidney and other urinary organs denoted the last estimate.
(3) Dose data lagged by two years for leukaemia excluding chronic lymphocytic leukaemia (CLL) and by 10 years for other cancers. For each cause of cancer death, the corresponding organ-absorbed dose was applied as listed in table 3.

with observed deaths $n = 319$; from 0.15 (−3.35, 5.20) to a negative ERR/Gy of −0.70 (−3.74, 3.87) for stomach cancer ($n = 218$) (table 4). The plots of the ERRs/Gy for almost all causes of death were closer to the vertical line of the origin with the smoking adjustment than without the smoking adjustment (figure 4). However, cancers with wide CIs showed inconsistent and unstable movements. The estimates for the colon ($n = 100$), prostate ($n = 39$) and kidney and other urinary organs ($n = 20$) were almost the same without or with the smoking adjustment. The estimates for the oesophagus ($n = 87$) and non-Hodgkin's lymphoma ($n = 34$) were not closer to zero with the smoking adjustment than without the smoking adjustment.

3.4. Smoking as a possible confounder between radiation and mortality

The United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) 2019 Report stated that alcohol consumption and smoking were suspected as important confounding factors that may have influenced the effects reported by the J-EPISODE (UNSCEAR 2019), citing Kudo *et al* (2018). In his editorial in the *Journal of Radiological Protection*, Akiba (2018) determined that the J-EPISODE confirmed a well-established principle of epidemiology, namely that smoking confounds the relationship between radiation and smoking-related disease risks when radiation is related to smoking.

Table 3 demonstrates the comparison of the estimated cancer mortality risk between the present and the previous study. For the 204 103 participants, the ERR/Gy for all cancers excluding leukaemia decreased when lung cancer was also excluded, as described in section 3.2. This decreasing tendency did not differ from the previous study using $H_p(10)$ (REA 2015).

When conducting a direct adjustment of smoking using pack-years for the subcohort, the ERR/Gy without the smoking adjustment decreased, as described in section 3.3. The most important feature of the J-EPISODE was the decreasing tendency of the ERR/Sv following adjustment for smoking (Kudo *et al* 2018). These decreasing trends remained unchanged even when the organ-absorbed dose was used, indicating the appropriateness of using organ-absorbed doses for further risk analysis.

Table 3. Reanalysis results of the cancer mortality risk using organ-absorbed dose for the J-EPISODE, in comparison with the previous study using recorded dose.

		Present study using organ-absorbed dose		Previous study using recorded dose in $H_p(10)$	
Cause of death	Organ dose	ERR/Gy	90% CI	ERR/Sv	90% CI
The Whole cohort of all 204 103 participants with the follow-up 1991–2010					
All cancers (ca) excluding leukaemia	Colon	1.22	(0.24, 2.26)	1.20	(0.43, 1.96)
All ca excluding lung ca and excluding leukaemia	Colon	0.50	(−0.56, 1.56)	0.66	(−0.18, 1.50)
Ca of oral cavity and pharynx	Oesophagus	−2.08	(−6.20[a], 5.03)	−0.44	(−4.68, 3.79)
Oesophageal ca	Oesophagus	2.37	(−2.12, 8.25)	3.20	(−0.37, 6.78)
Stomach ca	Stomach	0.96	(−1.24, 3.52)	0.50	(−1.23, 2.23)
Colon ca	Colon	−2.58	(−4.73, 0.52)	−1.64	(−4.02, 0.73)
Rectum ca	Colon	0.75	(−2.79, 5.57)	0.90	(−2.50, 4.29)
Liver ca	Liver	2.54	(−0.12, 5.67)	2.52	(0.33, 4.72)
Gallbladder ca	Gallbladder	−4.87	(−7.05[a], −1.15)	−3.51	(−6.06, −0.96)
Pancreatic ca	Pancreas	−5.29	(−7.21[a], −2.54)	−3.64	(−5.35, −1.92)
Lung ca	Lung	4.00	(1.81, 6.49)	3.15	(1.34, 4.96)
Prostate ca	Prostate	4.07	(−2.14, 13.31)	2.62	(−2.81, 8.04)
Bladder ca	Bladder	2.19	(−3.95, 13.02)	3.14	(−4.23, 10.51)
Ca of kidney and other urinary organs	Kidney	0.41	(−6.56[a], 12.98)	−0.13	(−5.25, 5.00)
Non-Hodgkin's lymphoma	Red bone marrow	11.35	(2.58, 23.70)	8.96	(1.30, 16.62)
Multiple myeloma	Red bone marrow	8.13	(−3.88, 30.68)	6.93	(−5.30, 19.15)
Leukaemia excluding CLL	Red bone marrow	−0.42	(−5.38, 7.59)	−0.27	(−4.07, 3.52)
The subcohort of 71 733 respondents to lifestyle surveys with follow-up 1999–2010					
All ca excluding leukaemia					
Without smoking adjustment	Colon	1.00	(−0.55, 2.82)	0.80	(−0.39, 2.19)
With smoking adjustment	Colon	0.25	(−1.16, 1.92)	0.29	(−0.81, 1.57)

(1) Dose data lagged by two years for leukaemia excluding chronic lymphocytic leukaemia (CLL) and by 10 years for other cancers. They were categorised into six groups in the analysis for the whole cohort and 14 groups for the subcohort.
(2) The CIs were based on the Wald method for the whole cohort and the likelihood method for the subcohort.
[a] Last estimate is denoted because the ERRs did not converge.

3.5. ERR and 90% CI by dose category for the subcohort

Figure 5 shows the ERR and 90% CI by dose category for the subcohort, i.e. the results from the direct adjustment using pack-years. The slope of the straight lines through the origin represents the ERR/Sv or ERR/Gy. The slope of the dotted line was ERR/Sv of 0.80 (90% CI: −0.39, 2.19) without the smoking adjustment using the recorded dose in $H_p(10)$ in the previous study (Kudo *et al* 2018). By contrast, in the present study, the dashed line demonstrated a ERR/Gy of 1.00 (−0.55, 2.82) without the smoking adjustment using the colon absorbed dose and this decreased to the solid line of ERR/Gy 0.25 (−1.16, 1.92) with the smoking adjustment.

3.5.1. Comparison of the CI results between using recorded dose (mSv) and organ dose (mGy)

In figure 5, the dot A shows a value of ERR 0.41 (−0.11, 0.93) at 261.9 mSv for the highest dose group of 200+ mSv in $H_p(10)$ on the dotted line (Kudo *et al* 2018). It shifted left to the dot B on the dashed line, the value of which is 0.44 (−0.29, 1.59) at 234.0 mGy in the colon absorbed dose group of 200+ mGy (table 5), and the CI is wider, because the magnitudes of the colon absorbed dose were approximately 0.8 times the recorded dose and the number of observed deaths also decreased from $n = 26$ in the 200+ mSv group to $n = 7$ in the 200+ mGy group. Conversely, the dot C (ERR −0.17 [−0.37, 0.03] at 136.9 mSv) in the group of 100–200 mSv on the dotted line moved up to the dot D (ERR −0.10 [−0.34, 0.21] at 133.1 mGy) in the group of 100–200 mGy on the dashed line but the CIs of both the dot C and D were almost the same width (table 5). This tendency of no differences in the CIs was also found in the lower dose groups less than 100 mSv or mGy. Accordingly, the slope of the dashed straight line was steeper than the dotted straight line, i.e. the ERR/Gy of 1.00 without the smoking adjustment was larger than the ERR/Sv of 0.80 without the smoking adjustment.

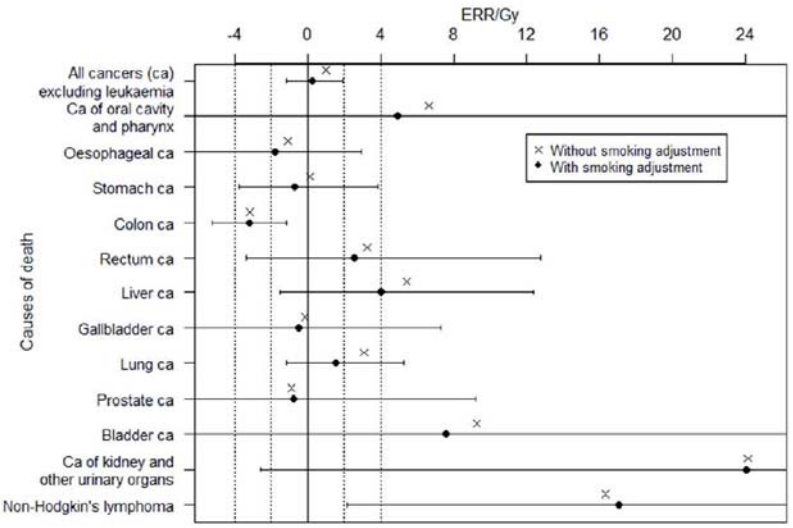

Figure 4. Comparison of ERR/Gy and 90% CI by causes of death for the subcohort of the J-EPISODE with follow-up in 1999–2010 with/without the smoking adjustment.
Note: (1) The ERR/Gy values for pancreatic cancer, multiple myeloma, and leukaemia excluding chronic lymphocytic leukaemia (CLL) were not converged.
(2) The CIs were based on the likelihood method, but those for oesophagus, colon, gallbladder, prostate and bladder were based on the Wald method. The lower bounds of the CIs for the oral cavity and pharynx, stomach and rectum denoted the last estimate of the likelihood method.
(3) Dose data lagged by two years for leukaemia excluding CLL and by 10 years for other cancers. For each cause of cancer death, the corresponding organ-absorbed dose was applied as listed in table 4.

Table 4. ERR/Gy and 90% CI by cause of death using organ-absorbed dose for the subcohort of the J-EPISODE with follow-up in 1999–2010.

		Without smoking adjustment		With smoking adjustment	
Causes of death	Organ dose	ERR/Gy	90% CI	ERR/Gy	90% CI
All cancers (ca) excluding leukaemia	Colon	1.00	(−0.55, 2.82)	0.25	(−1.16, 1.92)
Ca of oral cavity and pharynx	Oesophagus	6.66	(−7.45[b], 30.94)	4.94	(−7.86[b], 27.25)
Oesophageal ca	Oesophagus	−1.08	(−6.37, 4.21)[a]	−1.79	(−6.53, 2.96)[a]
Stomach ca	Stomach	0.15	(−3.35[b], 5.20)	−0.70	(−3.74[b], 3.87)
Colon ca	Colon	−3.17	(−4.14, −2.19)[a]	−3.16	(−5.19, −1.14)[a]
Rectum ca	Colon	3.25	(−2.61, 14.07)	2.55	(−3.38[b], 12.76)
Liver ca	Liver	5.44	(−0.66, 14.48)	4.05	(−1.50, 12.39)
Gallbladder ca	Gallbladder	−0.15	(−8.34, 8.05)[a]	−0.46	(−8.21, 7.30)[a]
Lung ca	Lung	3.09	(−0.11, 7.34)	1.56	(−1.15, 5.25)
Prostate ca	Prostate	−0.89	(−10.64, 8.87)[a]	−0.76	(−10.72, 9.21)[a]
Bladder ca	Bladder	9.26	(−17.29, 35.80)[a]	7.56	(−16.80, 31.91)[a]
Ca of kidney and other urinary organs	Kidney	24.11	(−2.45, 95.94)	24.01	(−2.55, 96.54)
Non-Hodgkin's lymphoma	Red bone marrow	16.32	(1.89, 45.30)	17.07	(2.18, 47.07)
All ca excluding lung ca and excluding leukaemia	Colon	0.51	(−1.20, 2.56)	−0.04	(−1.63, 1.88)

(1) The ERR/Gy values for pancreatic cancer, multiple myeloma and leukaemia excluding chronic lymphocytic leukaemia (CLL) were not converged.
(2) The CIs were based on the likelihood method.
(3) Dose data lagged by two years for leukaemia excluding CLL and by 10 years for other cancers.
[a] Wald-based CI.
[b] Last estimate is denoted because the ERRs did not converge.

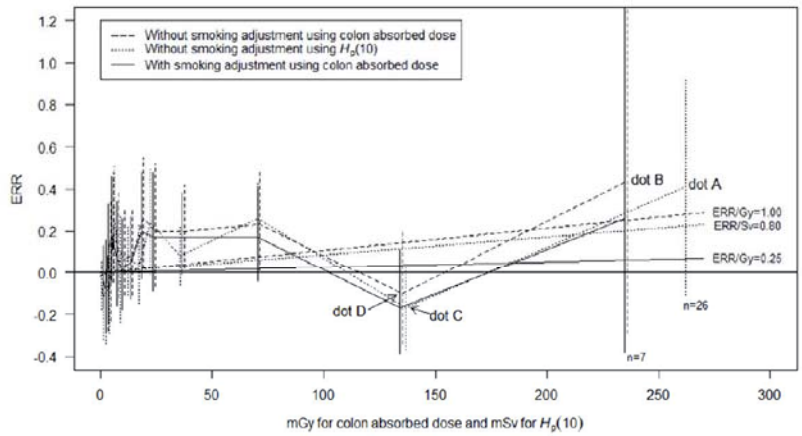

Figure 5. ERR and 90% CI for all cancers excluding leukaemia by dose category for the subcohort of the J-EPISODE with follow-up in 1999–2010 with the smoking adjustment using pack-years applied.
Note: Colon absorbed dose (mGy) and recorded dose (mSv) were categorised into 14 groups (0, >0, 1–, 2–, 3–, 5–, 7.5–, 10–, 15–, 20–, 25–, 50–, 100– and 200+). The slope of the straight lines through the origin represents ERR/Gy or ERR/Sv.

Table 5. ERR and 90% CI for all cancers excluding leukaemia by dose category for the subcohort of J-EPISODE with follow-up in 1999–2010 with/without the smoking adjustment using colon absorbed dose.

Dose category	Mean dose	Observed death	ERR and 90% CI without smoking adjustment	ERR and 90%CI with smoking adjustment
0 mGy	0.0 mGy	313	0.00	0.00
>0	0.4	188	−0.02 (−0.16, 0.14)	−0.03 (−0.17, 0.13)
1–	1.5	55	−0.08 (−0.28, 0.16)	−0.09 (−0.29, 0.16)
2–	2.5	41	0.02 (−0.23, 0.34)	0.02 (−0.24, 0.33)
3–	3.9	71	0.19 (−0.05, 0.48)	0.18 (−0.05, 0.46)
5–	6.2	60	0.11 (−0.12, 0.40)	0.07 (−0.16, 0.34)
7.5–	8.7	71	0.07 (−0.15, 0.32)	0.02 (−0.18, 0.26)
10–	12.3	106	0.08 (−0.11, 0.30)	0.05 (−0.13, 0.27)
15–	17.4	78	0.26 (0.02, 0.55)	0.20 (−0.03, 0.48)
20–	22.4	54	0.20 (−0.07, 0.52)	0.17 (−0.09, 0.48)
25–	35.4	145	0.20 (0.02, 0.42)	0.17 (−0.01, 0.38)
50–	69.4	103	0.23 (0.01, 0.48)	0.17 (−0.04, 0.41)
100–	133.1	34	−0.10 (−0.34, 0.21)	−0.17 (−0.39, 0.11)
200+	234.0	7	0.44 (−0.29, 1.59)	0.26 (−0.38, 1.26)
Previous analysis using recorded dose				
100– mSv	136.9*mSv*	61	−0.17 (−0.37, 0.03)	−0.22 (−0.41, 0.03)
200+	261.9	26	0.41 (−0.11, 0.93)	0.27 (−0.20, 0.74)

The CIs were based on the likelihood method.

3.5.2. ERR by dose category using organ dose with/without the smoking adjustment

Table 5 demonstrates that, for all dose groups, the ERRs without the smoking adjustment decreased to the values with the smoking adjustment. Accordingly, the slope of the solid straight line was less steep than that of the dashed straight line (figure 5), indicating the decreasing trend in the ERR/Gy with the smoking adjustment.

3.5.3. Sensitivity analysis using different organ dose category

Taking into consideration that estimates of ERR/Gy are susceptible to dose category, 14 dose groups (0, >0, 0.8–, 1.6–, 2.4–, 4–, 6–, 8–, 12–, 16–, 20–, 40–, 80– and 160+ mGy)—hereinafter called adjusted dose category—which had cut-off points 0.8 times the size of those of the dose category described in section 2.5.2, were temporarily applied in model (2). The estimated ERR/Gy of 1.09 (−0.47, 2.89) without the smoking

Table 6. ERR/Gy and ERR by dose category for all cancers excluding leukaemia for the subcohort of the J-EPISODE with follow-up in 1999–2010 with/without the smoking adjustment using colon absorbed dose when adjusted dose category was applied.

		Observed death	Without smoking adjustment	With smoking adjustment
			ERR/Gy and 90% CI	ERR/Gy and 90% CI
All cancers excluding leukaemia		1,326	1.09 (−0.47, 2.89)	0.41 (−1.02, 2.09)
Adjusted Dose category	Mean dose	Observed death	ERR and 90% CI	ERR and 90% CI
0 mGy	0.0 mGy	313	0.00	0.00
>0	0.3	175	−0.00 (−0.15, 0.17)	−0.01 (−0.15, 0.16)
0.8–	1.2	49	−0.15 (−0.35, 0.08)	−0.16 (−0.36, 0.07)
1.6–	2.0	34	−0.07 (−0.32, 0.24)	−0.06 (−0.31, 0.25)
2.4–	3.1	63	0.12 (−0.11, 0.40)	0.11 (−0.12, 0.39)
4–	5.0	66	0.34 (0.06, 0.67)	0.31 (0.04, 0.63)
6–	7.0	42	−0.07 (−0.30, 0.21)	−0.09 (−0.32, 0.18)
8–	9.9	104	0.09 (−0.10, 0.31)	0.04 (−0.14, 0.26)
12–	13.9	80	0.17 (−0.06, 0.43)	0.14 (−0.07, 0.40)
16–	17.9	57	0.18 (−0.08, 0.49)	0.13 (−0.12, 0.42)
20–	28.4	153	0.17 (−0.01, 0.38)	0.15 (−0.03, 0.35)
40–	56.3	129	0.32 (0.11, 0.57)	0.27 (0.06, 0.51)
80–	108.8	43	−0.16 (−0.37, 0.09)	−0.22 (−0.41, 0.01)
160+	197.3	18	0.47 (−0.04, 1.16)	0.34 (−0.13, 0.96)

(1) The cut-off points of the adjusted dose category were set as 0.8 times the size of those of the dose category in table 5.
(2) The CIs were based on the likelihood method.

adjustment decreased to 0.41 (−1.02, 2.09) with the smoking adjustment, but still demonstrated a decreasing tendency (table 6). The width of the CI of the ERR without the smoking adjustment in the highest dose group did not differ greatly, whether the dose unit was mSv or mGy. The ERR was 0.41 (−0.11, 0.93) at 261.9 mSv for the highest dose group of 200+ mSv in the previous study and 0.47 (−0.04, 1.16) at 197.3 mGy for the 160+ mGy group using the adjusted dose category, because the distribution of the observed deaths by the adjusted dose category in mGy was almost the same as in mSv. Regardless of the dose category, the decreasing trend in the ERR/Gy with the smoking adjustment remained.

3.6. Heterogeneity among the dose groups

The dose group of 15–20 mGy showed a relatively higher ERR, but the group greater than 100 mGy showed a lower ERR, even after the smoking adjustment (table 5). This trend was observed in both the whole cohort and the subcohort, as well as in many causes of deaths (not shown), suggesting that there unresolved heterogeneity might still exist among the dose groups in the J-EPISODE.

3.7. Association of smoking with cancer mortality

An association between smoking and lung cancer is one of the conditions of a confounder. By modifying model (2), we estimated the RRs and 90% CIs of the pack-years of smoking for lung cancer and all cancers excluding leukaemia by pack-years category (table 7). The RRs of lung cancer for smokers increased sharply over 30 pack-years. The lung cancer risk of current smokers with 30–50 pack-years, the proportion of which was the largest, was 5.4 times higher than that of non-smokers, whereas that of former smokers was 3.7 times higher. This result confirmed one of the requirements of confounding.

4. Discussion

4.1. Improved accuracy of dosimetry

Akiba (2018) indicated that the strengths of the J-EPISODE were its accurate dosimetry and virtually complete mortality follow-up. Regarding the first point, because the ICRP (2007) recommends the use of organ-absorbed doses for assessing cancer risk in epidemiological cohort studies, the J-EPISODE developed organ-absorbed dose conversion factors from dosimeter readings to further improve accuracy of dosimetry and to facilitate international comparisons of risk estimates (Furuta *et al* 2020a, 2020b, 2021).

In constructing the organ-absorbed doses, the doses received by the workers in the present study were assumed to derive predominantly from photon doses in the energy range of 100–3000 keV. The possibilities of neutron and internal exposures were discussed by Furuta *et al* (2021), as was the uncertainty regarding

Table 7. RR and 90% CI of pack-years of smoking by pack-year category as the reference being non-smoker for all cancers excluding leukaemia and lung cancer for the subcohort of the J-EPISODE with follow-up in 1999–2010 using organ-absorbed dose.

			All cancers excluding leukaemia		Lung cancer	
Pack-year category	Mean pack-years	Number of partcipants	Observed death	RR and 90% CI	Observed death	RR and 90% CI
Non-smoker	0	15 290	155	1	19	1
Current smoker						
>0	5.4	7494	21	2.21 (1.44, 3.40)	3	3.89 (1.37, 11.00)
10–	12.1	4059	9	0.87 (0.49, 1.54)	0	—
15–	17.1	4403	43	2.40 (1.79, 3.22)	7	2.92 (1.37, 6.22)
20–	22.1	4386	60	2.28 (1.76, 2.94)	9	2.68 (1.36, 5.29)
25–	27.0	4129	68	1.99 (1.56, 2.54)	11	2.57 (1.37, 4.84)
30–	37.7	12 063	340	2.27 (1.93, 2.67)	99	5.38 (3.54, 8.16)
50+	63.9	4963	258	3.01 (2.54, 3.57)	82	7.61 (4.98, 11.62)
Former smoker						
>0	5.2	3228	29	1.29 (0.84, 1.97)	4	1.38 (0.47, 4.04)
10–	11.9	1922	26	1.38 (0.91, 2.09)	4	1.67 (0.60, 4.66)
15–	17.1	1736	28	1.37 (0.93, 2.03)	5	2.00 (0.80, 5.00)
20–	22.1	1590	42	1.87 (1.34, 2.61)	5	1.73 (0.70, 4.27)
25–	26.9	1166	25	1.33 (0.91, 1.94)	4	1.66 (0.64, 4.30)
30–	37.9	3382	125	1.89 (1.51, 2.36)	32	3.74 (2.20, 6.37)
50+	70.4	1924	97	2.09 (1.66, 2.63)	35	5.76 (3.47, 9.54)

The CIs were based on the Wald method.

photon dosimetry. Ultimately, the organ-absorbed dose reconstruction in the J-EPISODE ignored the neutron and internal exposure doses, if any.

4.2. Improved risk estimates by using the organ-absorbed dose

When over- or underestimates were found in the dose measurements, the risk estimates reflected such evaluation. In the IARC Three-Country Study including the United States, the UK and Canada, organ doses were constructed by overcoming the uncertainty in dosimetry (Fix *et al* 1997). The dose committee concluded that for solid cancers, the recorded dose and organ dose were compatible, but for leukaemia, the recorded dose overestimated the RBM absorbed dose by approximately 20%. Cardis *et al* (1995) evaluated the ERR/Sv for all cancers excluding leukaemia as is, which was computed using the recorded dose, but evaluated the risk of leukaemia to be 20% higher than the computed ERR/Sv. In the following 15-Country Study, organ-absorbed dose was used for the risk estimation. Regarding the effect of dose reconstruction on risk estimates in the INWORKS, the ERR/Gy for all cancers excluding leukaemia using colon doses was 0.48 (0.20, 0.79), while the ERR/Sv for the analysis using recorded photon doses was as low as 0.35 (0.14, 0.57) (Richardson *et al* 2015). The use of colon doses, which were also adjusted for errors, did not improve the fit of the model, but the comparison with the LSS became easier by using organ dose. In the subcohort of the J-EPISODE, the risk estimate for the model without the smoking adjustment using recorded doses increased from ERR/Sv 0.80 (−0.39, 2.19) to ERR/Gy 1.00 (−0.55, 2.82) when organ doses were used (table 3). This was a logical consequence of the fact that recorded doses were overestimated in terms of organ doses.

4.3. Smoking-adjusted radiation risk

As described in section 3.4, it was not surprising to see in table 3 that the ERR/Gy for cancer was slightly higher than the ERR/Sv based on recorded dose because the recorded dose was generally overestimated. However, for all cancers excluding leukaemia, when excluding lung cancer in the whole cohort and conducting smoking adjustment in the subcohort, the opposite trend may be seen. In the whole cohort, the lung-cancer-excluded ERR/Gy of 0.50 (−0.56, 1.56) in the present study was lower than the lung-cancer-excluded ERR/Sv of 0.66 (−0.18, 1.50) in the previous study for all cancers excluding leukaemia. This was because the risk estimate using organ doses (ERR/Gy 4.00 [1.81, 6.49]) for lung cancer, which accounted for 22% of the observed deaths, increased largely compared with that using the recorded dose case (ERR/Sv 3.15 [1.34, 4.96]) (table 3). Eventually, the results of excluding lung cancer in the present analysis showed a decrease from the previous study. In the subcohort, the smoking-adjusted ERR/Gy of 0.25 (−1.16, 1.92) in the present study for all cancers excluding leukaemia was slightly lower than the smoking-adjusted ERR/Sv of 0.29 (−0.81, 1.57) in the previous study. However, by comparing the smoking-adjusted risk in the subcohort between using recorded doses and organ doses for lung cancer ($n = 319$), stomach cancer

Table 8. Indirect validation of smoking confounding by excluding lung cancer from all cancers excluding leukaemia.

Cause of cancer death	Observed deaths	Radiation risk
15-Country Collaborative Study		
Cardis *et al* (2007)		ERR/Sv and 90% CI
All cancers (ca) excluding leukaemia	5024	0.97 (0.27, 1.80)
All ca excluding leukaemia and excluding lung ca and pleura ca	3528	0.59 (−0.16, 1.51)
Lung ca	1457	1.86 (0.49, 3.63)
Pleura ca	39	5.28 (<0, 39.9)
INWORKS		
Richardson *et al* (2015, 2017)		ERR/Gy and 90% CI
All ca excluding leukaemia	19 064	0.48 (0.20, 0.79)
Solid ca	17 957	0.47 (0.18, 0.79)
Solid ca (simple model [a])	17 957	0.37 (0.14, 0.62)
Solid ca excluding lung ca	12 155	0.46 (0.11, 0.85)
Solid ca excluding lung ca (simple model)	12 155	0.35 (0.07, 0.65)
Lung ca	5802	0.51 (0.00, 1.09)
The subcohort of the J-EPISODE with the smoking adjustment using organ dose		ERR/Gy and 90% CI
All ca excluding leukaemia	1326	0.25 (−1.16, 1.92)
All ca excluding leukaemia without smoking adjustment	1326	1.00 (−0.55, 2.85)
All ca excluding leukaemia with DOE [b] adjustment	1326	0.76 (−0.86, 2.71)
All ca excluding leukaemia and excluding lung ca without smoking adjustment	1007	0.51 (−1.20, 2.56)
Lung ca	319	1.56 (−1.15, 5.25)
Lung ca without smoking adjustment	319	3.09 (−0.11, 7.34)
Lung ca with DOE adjustment	319	4.05 (0.19, 9.60)
French combined cohort		
Metz-Flamant *et al* (2013)		ERR/Sv and 90% CI
All solid ca	2312	0.34 (−0.56, 1.38)
All solid ca without SES [c] adjustment	2312	1.47 (0.40, 2.67)
Lung ca	585	1.20 (−0.63, 3.55)
UK updated third NRRW		
Haylock *et al* (2018)		ERR/Sv and 90% CI
All ca excluding leukaemia	11 329	0.29 (0.06, 0.53)
All ca excluding leukaemia and excluding lung ca and pleura	8114	0.37 (0.11, 0.65)
Ca from tracher, bronchus and lung	3058	0.03 (−0.38, 0.51)
Pleura ca	157	1.06 (−0.96, 5.21)
Pooled U.S. cohort		
Schubauer-Berigan *et al* (2015)		ERR% per 10 mSv and 95% CI [d]
All ca excluding leukaemia	10 877	0.14 (−0.17, 0.48)
Lung ca	3514	0.07 (−0.43, 0.66)
Smoking-related ca excluding leukaemia	6950	−0.08 (−0.43, 0.32)

[a] Adjusted only for country, age, sex and birth cohort.
[b] Duration of employment.
[c] Socioeconomic status.
[d] Based on total (gamma, neutron and tritium) dose.

($n = 218$) and liver cancer ($n = 138$), which contributed largely to the number of deaths, the estimated risk value moved away from 0 for lung cancer (from ERR/Sv 0.94 [−1.24, 3.90] to ERR/Gy 1.56 [−1.15, 5.25]), stomach cancer (from −0.20 [−2.94, 2.55] to −0.70 [−3.74, 3.87]) and liver cancer (from 3.89 [−2.94, 2.55] to 4.05 [−1.50, 12.39]), respectively (REA 2015; table 4). The trend by cancer site was not necessarily the same as that for all cancers excluding leukaemia. Therefore, the decrease found in all cancers excluding leukaemia may be coincidental.

4.4. Indirect validation of smoking as a confounder by excluding lung cancer

All cohort studies were concerned about smoking as a possible confounder, but because of the few cohorts with information on smoking status, an indirect method was used to examine the possibility of smoking as a confounder by excluding lung cancer from all cancers (table 8). In the 15-Country Study, the ERR/Sv 0.97

(0.27, 1.80) for all cancers excluding leukaemia decreased to 0.59 (−0.16, 1.51) when lung and pleura cancers were excluded (Cardis *et al* 2007). This tendency was similar to the J-EPISODE. In the subcohort of the J-EPISODE, the ERR/Gy for all cancers excluding leukaemia without the smoking adjustment was 1.00 (−0.55, 2.85), whereas that for all cancers excluding leukaemia and excluding lung cancer without the smoking adjustment was 0.51 (−1.20, 2.56). On the contrary, in the INWORKS, the ERR/Gy for solid cancers was 0.47 (0.18, 0.79) and solid cancers excluding lung cancer also had an ERR/Gy of 0.46 (0.11, 0.85), which were essentially the same value (Richardson *et al* 2015). Therefore, they concluded that the values suggested no confounding by smoking in the INWORKS. However, the difference in these results when lung cancer was excluded was considered to be due to the magnitude of the ERR for lung cancer. In the INWORKS, the ERR/Gy for lung cancer was 0.51 (0.00, 1.09) (Richardson *et al* 2017), which was almost the same as that for solid cancers. On the contrary, in the 15-Country Study, the ERR/Sv for lung cancer was 1.86 (0.49, 3.63), which was almost twice greater than that for all cancers excluding leukaemia (Cardis *et al* 2007). In the subcohort of the J-EPISODE, the ERR/Gy for lung cancer without the smoking adjustment was 3.09 (−0.11, 7.34), almost three times greater than that for all cancers excluding leukaemia.

Despite the uniformity of the ERRs/Gy by cancer site in the INWORKS results, the country cohorts of France, the UK and the United States displayed different results from that of the pooled cohort, although differences in the facilities included and observation periods were found. In the French combined cohort that consisted of the Commissariat à l'Energie Atomique (CEA), AREVA Nuclear Cycle (AREVA NC) and Electricité de France (EDF), the ERR/Sv for all solid cancers was 0.34 (−0.56, 1.38), which is positive but not significant, whereas that for lung cancer was 1.20 (−0.63, 3.55) (Metz-Flamant *et al* 2013). The result after excluding lung cancer was not shown, but might be decreased. In the main analyses, socioeconomic status (SES) was adjusted, partially considering smoking habits. When SES was not adjusted, the ERR/Sv for all solid cancers increased to 1.47 (0.40, 2.67). In the pooled U.S. cohort from five facilities, namely Hanford, Idaho National Laboratory (INL), Oak Ridge National Laboratory (ORNL), Portsmouth Naval Shipyard (PNS) and Savannah River Site (SRS), the ERR% per 10 mSv and 95% CI for all cancers excluding leukaemia was 0.14 (−0.17, 0.48), which was positive but not significant, whereas that for lung cancer was 0.07 (−0.43, 0.66) (Schubauer-Berigan *et al* 2015). The results of a study on chronic obstructive pulmonary disease (COPD), which is highly influenced by smoking, indicated that confounding by smoking may be positive in Hanford and ORNL and negative in INL, PNS and SRS. A strong healthy worker survival effect (HWSE) was also identified as a feature of the pooled cohort, but the adjusted increase in ERR in HWSE was highest for smoking-related cancers. In the main analysis, SES (first job title) and duration of employment (DOE) were used as adjustment variables, which may have partially adjusted for the smoking effect along with HWSE. In the UK updated third analysis of National Registry for Radiation Workers (NRRW), including the Ministry of Defence, British Nuclear Fuels (BNFL), UK Atomic Energy Authority (UKAEA), British Energy Generation and Magnox Electric and Atomic Weapons Establishment, the ERR/Sv of 0.37 (0.11, 0.65) for all cancers excluding leukaemia and excluding lung and pleura cancers increased from 0.29 (0.06, 0.53) for all cancers excluding leukaemia (Muirhead *et al* 2009, Haylock *et al* 2018). Considering the low estimate of 0.03 (−0.38, 0.51) for lung cancer, some negative confounding effect of smoking on radiation risk estimates was indicated. The results indicate that when examining smoking as a confounder, not only smoking adjustment but also the relationship with other risk factors such as adjustment variables, that is, stratification variables, should be fully considered in the model.

4.5. Possible healthy worker survivor effects

The INWORKS estimated the risk in the main analysis by adding SES related to job, DOE and neutron monitoring status as adjustment variables to the simple model that adjusted only for country, age, sex and birth cohort. Possible confounding by SES and DOE was also examined by excluding each variable from the model. The results suggested that job position positively confounded the results but DOE negatively confounded the results because of HWSE (Cardis *et al* 2007, Richardson *et al* 2015). The estimated ERR/Gy for solid cancers from the simple model was 0.37 (0.14, 0.62), and that for solid cancers excluding lung cancer was 0.35 (0.07, 0.65), whereas the estimates from the fully adjusted model were 0.47 (0.18, 0.79) and 0.46 (0.11, 0.85), respectively (table 8), indicating that the net adjustment effect by SES and DOE was small (Richardson *et al* 2015). This may be due to the offsetting of the positive confounding by job position and negative confounding by DOE. As the J-EPISODE lacks information on job position, we could not conduct an analysis with both SES and DOE as adjustment variables under the same condition as that in the INWORKS. Even though interpretation of the risk estimates is difficult, the results when only DOE was adjusted are presented in table 9. The DOE-adjusted risk estimates of 0.76 (−0.86, 2.71) largely increased compared with the DOE-non-adjusted estimates of 0.25 (−1.16, 1.92), which suggests that DOE is a negative confounder. These results were similar with those obtained using recorded dose in the study of Kudo *et al*

Table 9. ERR/Gy and 90% CI by cause of death for the subcohort of the J-EPISODE with follow-up in 1999–2010 using organ-absorbed doses when the duration of employment was added as the adjustment variable in the model.

	Without smoking adjustment		With smoking adjustment	
Causes of death	ERR/Gy	90% CI	ERR/Gy	90% CI
All cancers (ca) excluding leukaemia	1.78 [1.00]	(−0.04, 3.96)	0.76 [0.25]	(−0.86, 2.71)
Ca of oral cavity and pharynx	16.10 [6.66]	(−2.08, 59.66)	12.75 [4.94]	(−3.9[b], 51.59)
Oesophageal ca	−1.42 [−1.08]	(−6.54, 3.70)[a]	−2.19 [−1.79]	(−6.60, 2.23)[a]
Stomach ca	−0.26 [0.15]	(−4.05[b], 5.07)	−1.25 [−0.70]	(−4.43[b], 3.36)
Colon ca	−3.16 [−3.17]	(−5.47, −0.85)[a]	−3.17 [−3.16]	(−3.81, −2.53)[a]
Rectum ca	6.35 [3.25]	(−1.66, 22.40)	5.30 [2.25]	(−2.12, 20.56)
Liver ca	13.19 [5.44]	(3.31, 28.71)	10.25 [4.05]	(1.47, 24.30)
Gallbladder ca	−0.37 [−0.15]	(−8.87, 8.12)[a]	−0.51 [−0.46]	(−8.71, 7.69)[a]
Lung ca	6.29 [3.09]	(1.70, 12.76)	4.05 [1.56]	(0.19, 9.60)
Prostate ca	−3.52 [−0.89]	(−8.68, 1.64)[a]	−3.51 [−0.76]	(−8.74, 1.72)[a]
Bladder ca	23.76 [9.26]	(−28.20, 75.73)[a]	26.91 [7.56]	(−31.30, 85.13)[a]
Ca of kidney and other urinary organs	35.67 [24.11]	(−1.01, 144.7)	36.92 [24.01]	(−1.02, 152.5)
Non-Hodgkin's lymphoma	21.64 [16.32]	(3.17, 63.46)	23.44 [17.01]	(3.82, 68.15)

(1) Figures in bracket represent the ERR/Gy in table 4, where the duration of employment was not adjusted.
(2) The CIs were based on the likelihood method.
[a] Wald-based CI.
[b] Last estimate is denoted because the ERRs did not converge.

(2018). The third lifestyle survey, conducted between 2015 and 2019, added SES-related questions on employer type, company size, job type and final job position to allow for a more detailed analysis of confounding factors.

4.6. Comparison of risk estimates with other studies

Richardson *et al* (2015) reported that the results of the INWORKS were statistically compatible with the LSS. The ERR/Gy and 90% CI for solid cancers was 0.47 (0.18, 0.79) in the INWORKS (table 8), whereas the ERR/Sv for men aged 20–60 years in the LSS was 0.32 with 95% CI 0.01–0.05. Furthermore, Leuraud *et al* (2021) emphasized that by restricting the comparison by using similar ages and follow-up periods, they found complementary results from different studies with ERR/Gy of 0.28 (0.18, 0.38) for the LSS and 0.29 (0.07, 0.53) for the INWORKS.

On the contrary, the results of the subcohort of the J-EPISODE were not statistically significant for all cancers excluding leukaemia (0.25 [−1.16, 1.92]) owing to the lack of person-years, but the point estimate of the ERR/Gy 0.25 was within the 90% CI 0.20–0.79 of ERR/Gy of 0.48 for all cancers excluding leukaemia in the INWORKS. Further accumulation of person-years of follow-up is expected for proper comparison.

5. Conclusion

The J-EPISODE established organ-absorbed doses from the recorded doses by using the organ dose reconstruction methods to improve the accuracy of dosimetry. The estimated ERRs/Gy for cancer mortality were consistent with the previous analysis results using $H_p(10)$, indicating that the risk estimation using the organ-absorbed dose was applicable for the J-EPISODE. In the whole cohort, all cancers excluding leukaemia, lung cancer and non-Hodgkin's lymphoma had statistically significant positive ERR/Gy estimates; leukaemia excluding CLL had negative but not statistically significant estimates. Gallbladder cancer and pancreatic cancer showed statistically significant negative. The main features related to smoking as a confounder reported in the previous analysis remained unchanged. In the subcohort, for almost all causes of death such as lung cancer and stomach cancer, the estimated ERR/Gy decreased by the smoking adjustment, although those for the colon, prostate and kidney and other urinary organs were almost the same after the adjustment. These results indicate that confounding by smoking seriously biased the radiation risk estimate in the J-EPISODE and thus should be accounted for even if organ dose is used. The J-EPISODE will also use organ-absorbed doses to analyse the cancer incidence, which has become available.

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Paper

Organ Dose Reconstruction Applicable for a Japanese Nuclear Worker Cohort: J-EPISODE

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Abstract—**An evaluation of cancer risk based on organ-absorbed dose is underway for the Japanese Epidemiological Study on Low-Dose Radiation Effects (J-EPISODE), which has analyzed health effects in association with radiation exposure evaluated with the personal dose equivalent $H_p(10)$. Although the concept of effective dose and its operational definition of $H_p(10)$ are widely used for radiological protection purposes, effective dose is not recommended for epidemiological evaluation. Organ-absorbed dose was instead adopted for the IARC 15-Country Collaborative study (15-Country study), the International Nuclear Workers Study (INWORKS), the Mayak worker study, and the Life Span Study (LSS) of atomic bomb survivors. The reconstruction method in J-EPISODE followed in principle the approach adopted in the 15-Country Study. As part of the approach of J-EPISODE, a conversion factor from photon dosimeter reading to air kerma was developed using dosimeter response data, which were measured by the experiment using an anthropomorphic phantom, and it was confirmed that the 15-Country study's assumption of photon energy and geometry distribution in a work environment applied to Japanese nuclear workers. This article focuses on a method for reconstructing the conversion factor from photon dosimeter reading to organ-absorbed photon dose for a Japanese nuclear worker cohort. The model for estimating the conversion factor was defined under the assumption of a lognormal distribution from three concerned bias factors: (1) a dosimeter reading per air kerma, i.e., dosimeter response; (2) an organ-absorbed dose per air kerma; and (3) a factor relating to the differences in dose concepts and calibration practices between the roentgen dosimeter era and the present. Dosimeter response data were cited from the companion paper. Data on organ-absorbed photon dose per air kerma were estimated using a voxel phantom with the average Japanese adult male height and weight. The bias factor for the recorded dose in the roentgen era was defined, considering the backscatter radiation from the human body. The estimated values of organ-absorbed photon dose per air kerma were almost the same as those in ICRP Publication 116, revealing that the effect of differences in body size was almost negligible. The conversion factors from dosimeter reading to organ-absorbed dose were estimated by period (the roentgen era or from then), nuclear facility type (nuclear power plant or other), dosimeter type, and tissue or organ. The estimated conversion factors ranged from 0.7 to 0.9 (Gy Sv^{-1}). The estimated cumulative organ-absorbed photon dose for the participants of J-EPISODE demonstrated that organ-absorbed dose values were approximately 0.8 times the recorded doses if neglecting dose-unit differences. J-EPISODE reconstructed an organ-absorbed dose conversion factor and will evaluate the risk of cancer mortality and morbidity using the organ-absorbed dose in the future.**

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Key words: dose, organ; dosimetry, external; epidemiology; nuclear workers

INTRODUCTION

The needs of organ-absorbed dose

Although the concept of effective dose E and its operational definition of personal dose equivalent $H_p(10)$ are now widely used for radiological protection purposes, the International Commission on Radiological Protection (ICRP) has stated that effective dose is not recommended for epidemiological evaluation (ICRP 2007). It is instead desirable to use organ-absorbed dose for the evaluation of cancer risk in epidemiological cohort studies. Organ-absorbed dose, which is suitably weighted by the relative biological effectiveness (RBE), if necessary, when dealing with neutrons, was adopted for the 15-Country Collaborative Study (hereinafter called the 15-Country study) conducted by the International Agency for Research on Cancer (IARC) (Cardis et al. 2007; Thierry-Chef et al. 2007; Vrijheid et al. 2007). It was also used in the

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International Nuclear Workers Study (INWORKS) (Leuraud et al. 2015; Thierry-Chef et al. 2015; Richardson et al. 2015; Hamra et al. 2016), the Mayak worker study (Gilbert et al. 2013), and the Life Span Study (LSS) of atomic bomb survivors, which used RBE-weighted absorbed dose for neutrons (Preston et al. 2007; Ozasa et al. 2012; Grant et al. 2017).

Preceding studies on organ-absorbed dose reconstruction

In the IARC Combined Study, which consisted of seven cohorts in Canada, the United Kingdom, and the United States, Fix et al. (1997) conducted a detailed study of dosimetry technology, radiation fields, and measurement practices, followed by conversion of externally recorded doses to organ-absorbed doses [lung dose and red bone marrow (RBM)]. Thierry-Chef et al. (2007) conducted a study on dose errors within the framework of the 15-Country study and outlined details of the organ-absorbed dose reconstruction method. Thierry-Chef et al. (2015) updated and developed the same method for the INWORKS, which was also an IARC study. Additionally, the Million Worker Study (MWS) also implemented various organ-absorbed dose reconstructions (Bouville et al. 2015). Among these studies, Thierry-Chef et al. (2007) described the method in the most comprehensive and practical detailed manner; therefore, it was used in this study.

Framework for reconstructing the organ-absorbed dose in the 15-Country study

The framework for organ-absorbed dose reconstruction established in the 15-Country study consisted of four main components, as described in Thierry-Chef et al. (2007): (1) experiments of dosimeter response employing readings per $H_p(10)$ for three dosimeter types used until 2000 (the old film badge [FB], a multi-element FB, and a thermoluminescence dosimeter [TLD]); (2) an assumption concerning photon energy and geometry distribution in the workplace; (3) a conversion coefficient from $H_p(10)$ to an organ-absorbed dose derived from ICRP Publication 74 (ICRP 1996); and finally (4) the construction of a conversion factor from dosimeter readings to organ-absorbed dose using the above results in a mathematical model.

Framework for reconstructing the organ-absorbed dose in the J-EPISODE

The Japanese Epidemiological Study on Low-Dose Radiation Effects (J-EPISODE) has been conducted by the Radiation Effects Association (REA) since 1990 and analyzed health effects in association with radiation exposure evaluated with the personal dose equivalent $H_p(10)$ (REA 2015; Kudo et al. 2018a and b). However, among internationally-evaluated radiation epidemiological studies, the organ-absorbed dose has been mainly used for the evaluation of morbidity and mortality due to cancer. For the J-EPISODE to be compared and evaluated internationally in the future, it is indispensable for it to use an organ-absorbed dose. Additionally, cancer incidence data since 2016 have become available from the National Cancer Registry (Matsuda and Sobue 2015). These conditions have enhanced the J-EPISODE reconstruction of an organ-absorbed dose, and the Expert Committee on Reconstruction of Organ Dose (membership: Michiaki Kai, Norio Tsujimura, Kaoru Sato, and Norihito Sato) was set up within the REA during the fiscal year 2017–2018 (REA 2019). The framework for the conversion from a dosimeter reading to an organ-absorbed dose is displayed in Fig. 1.

The report by the Expert Committee is summarized as follows (REA 2019):

1. The 15-Country study examined the dosimeter response to photon exposure for the dosimeter types FB and TLD. To supplement data for the dosimeter types recently in use, the J-EPISODE experimented on the dosimeter response for radio-photoluminescent glass dosimeters (glass badges [GBs]), active personal dosimeters (hereinafter called electronic personal dosimeter [EPDs]), and optically stimulated luminescence dosimeters (Luminess badges [LBs]) using a device that irradiated an anthropomorphic phantom in the Japan Atomic Energy Agency (JAEA) calibration laboratories, as described by Furuta et al. (2020a). The obtained data were consistent with those in the 15-Country study;
2. The reconstruction of an organ-absorbed dose necessitated information on the photon energy and geometry distribution of the exposed population. The J-EPISODE employed the 15-Country study's assumption concerning photon energy and geometry distribution in a work environment. Simultaneously, to verify the validity of the 15-Country study's assumption in Japan, a literature survey was conducted to review documents on the work environments of Japanese nuclear power plants (NPPs). The literature survey disclosed that Japanese electric power companies had jointly researched energy distribution and incidence direction distribution of gamma rays in the workplace during periodic inspections and maintenance, as well as during plant operation, in the 1980s. The analysis of the survey results on photon energy and geometry distribution at Japanese NPPs demonstrated the appropriateness of applying the 15-Country study's assumption for nuclear workers in Japan and reconstructing an organ-absorbed dose in J-EPISODE, as also described by Furuta et al. (2020b);
3. The 15-Country study applied the conversion factor of an organ-absorbed dose per $H_p(10)$ derived from the conversion coefficient in ICRP Publication 74 (ICRP 1996), which was based on the Reference Computational Phantom-Adult Male (RCP-AM) with standard Caucasian physiques defined in ICRP Publication 110

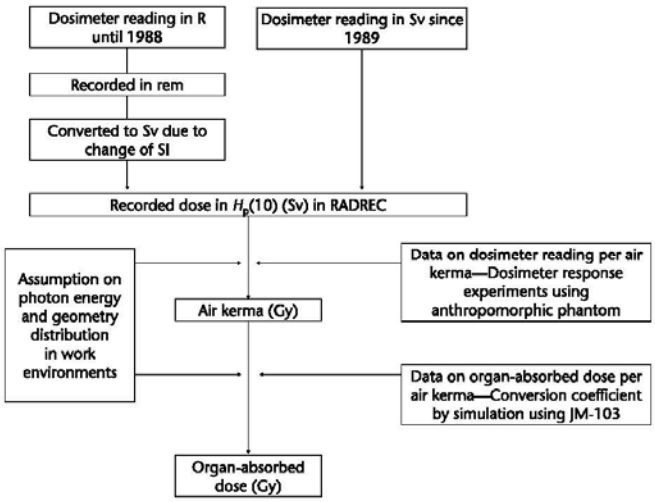

Fig. 1. Framework of reconstruction from dosimeter reading to organ-absorbed dose adopted for the J-EPISODE.

(ICRP 2009). The INWORKS also employed the updated conversion coefficients in ICRP Publication 116 (ICRP 2010). In contrast, the J-EPISODE estimated a conversion coefficient from air kerma to an organ-absorbed dose based on JM-103, an adult male voxel phantom with average Japanese size (Sato et al. 2010, 2011; Sato and Takahashi 2012, 2017; Manabe et al. 2014) that was developed by the JAEA based on ICRP Publication 110 (ICRP 2009); and

4. The above results were integrated using a mathematical model of a lognormal distribution. Finally, the conversion factor from dosimeter reading to organ-absorbed dose was constructed.

Aim of the study

The present study aimed to describe 3. and 4. above and to reconstruct organ-absorbed photon doses from photon dosimeter readings taken from 1957 to 2010 from the J-EPISODE participants. The goal was to reanalyze the data for evaluating radiation risk and confirm the appropriateness of the conversion factors. This manuscript focuses on the conversion from external photon doses only; it briefly addresses other possible sources of radiation exposure for nuclear workers in Japan.

MATERIALS AND METHODS

Study subjects and recorded dose of the J-EPISODE

The J-EPISODE targeted occupationally exposed workers registered with the Radiation Dose Registration Center (RADREC) (Asano and Ito 2019) within the REA, which included workers in nuclear energy research and development (R&D), nuclear fuel processing, and employed in NPPs, as well as contractors and subcontractors working in NPPs. Each nuclear facility regularly submitted the records of individual annual doses, which were received in the facility and evaluated in $H_p(10)$, to the RADREC. The J-EPISODE was provided with the individual annual doses received in each nuclear facility from 1957 to 2010. This study assumed that the recorded doses were predominantly derived from the photon external exposure with an energy between 100 keV and 3,000 keV.

Model for estimating conversion factors

The model for estimating conversion factors from dosimeter readings to organ-absorbed doses was defined as the following:

$$D_R = T \times B_1 \times B_2 \times B_3, \quad (1)$$

where D_R was the dosimeter reading, T was the organ-absorbed dose, and B_i was the bias factor (i = 1, 2, and 3). B_1 was a reciprocal of the organ-absorbed dose per air kerma, B_2 a dosimeter reading per air kerma, and B_3 a factor relating to the differences in dose concepts and calibration practices. It was considered that T was a true value and that D_R was a measured value including biases. Here, it was assumed that the variables B_1, B_2, and B_3 followed a lognormal distribution for the convenience of calculation:

$$\text{Bias } B_i \sim LN\left(m_i, s_i^2\right), \quad (2)$$

where m_i was the mean of the natural logarithm (ln) of each factor B_i: $\ln(B_i)$, and s_i was the standard deviation of $\ln(B_i)$.

Then, the overall bias B, the products of B_1, B_2, and B_3, also followed a lognormal distribution, as described in the Appendix of the present paper:

$$\text{Overall bias } B \left(= B_1 \times B_2 \times B_3\right) \sim LN\left(m, s^2\right), \quad (3)$$

where m was the sum of the means of $\ln(B_i)$: $m = \Sigma m_i$, and s^2 was the sum of the variances of $\ln(B_i)$: $s^2 = \Sigma s_i^2$.

The bias uncertainty K_i was defined for each bias factor B_i, as follows:

$$K_i = \exp(1.96 \times s_i). \quad (4)$$

Therefore, the 95% confidence interval for the estimated bias B_i was the interval of $(B_i/K_i, B_i \times K_i)$.

The overall uncertainty K of the overall bias B was expressed as the following:

$$K = \exp(1.96 \times s) = \exp\left\{1.96 \times \text{sqrt}\left[\Sigma \left(\ln K_i/1.96\right)^2\right]\right\}. \quad (5)$$

The conversion factor c between the dosimeter reading D_R and the organ-absorbed dose T was expressed as the mean of the overall bias B:

$$c = E(B) = \exp\left(m + s^2/2\right) = \exp(m) \times \exp\left(s^2/2\right). \quad (6)$$

The conversion factor c was a constant determined by the period (until 1988 or since 1989), nuclear facility type (NPP or mixed-activities [MA] facility such as R&D organization and fuel processing factory), dosimeter type, and tissue or organ.

The organ-absorbed dose estimated by this method had the following characteristics. The mean value of the estimated organ-absorbed dose (D_R/c) obtained by dividing the recorded dose of each worker by the conversion factor c was equal to the mean value of the true organ-absorbed dose, i.e. an unbiased estimation value. The following equation holds for each year, nuclear facility, and tissue or organ:

$$E(D_R/c) = E(D_R)/c = E(T) \times E(B)/c = E(T). \quad (7)$$

The estimated organ-absorbed dose obtained by dividing the recorded dose for each worker by the conversion factor c should not be interpreted as the organ-absorbed dose for each worker because differences in body size among workers were not taken into consideration. The estimated organ-absorbed dose for a specific worker assumed that the exposure dose followed the same photon energy and geometry distribution as the average of the workers at the nuclear facility and that the body size was the same as the Japanese average.

The uncertainty of the conversion factor c was the same as the overall uncertainty K.

Distribution of photon energy and geometry at the working environment

This study employed the 15-Country study's assumption of photon energy and geometry distribution at workplaces (Thierry-Chef et al. 2007): on average, in NPPs, 10% of the dose received by nuclear workers was due to photon energies ranging from 100 to 300 keV and 90% was from photon energies ranging from 300 to 3,000 keV. In MA facilities, 20% of the dose received by workers was from photon energies ranging from 100 to 300 keV and 80% was from photon energies ranging from 300 to 3,000 keV, with the average geometry being 50% in the antero-posterior (AP) and 50% in the isotropic (ISO) geometry for NPPs and MA facilities. Furuta et al. (2020b) stated that the literature survey results in Japan provided strong evidence that supported the robustness and generality of the 15-Country study's assumption, which was estimated based on the judgments of experts at nuclear facilities around the world.

According to the 15-Country study (Thierry-Chef et al. 2007), the dosimeter response in the 100–300 keV range was considered to be represented by the responses at 118 and 208 keV—the mean energy of beam code N-150 and N-250, respectively—in the experiment. Although this study used responses at 119 and 207 keV, the differences in the mean energy were negligible. Therefore, the dosimeter response in the 100–300 keV range was computed on the weighted average, 25% of which was for the responses at 119 keV and 75% for the responses at 207 keV. In addition, the dosimeter response in the 300–3,000 keV range was considered to be represented by a point at 662 keV. The results representing the energy range of 100–300 keV and 300–3,000 keV were then averaged in the same way for estimating the conversion factor.

B_1 and K_1: Conversion coefficient of an organ-absorbed dose from air kerma for JM-103

The basic data of bias factor B_1 were the reciprocal of the organ-absorbed dose per air kerma by photon energy and geometry. The use of a Japanese adult male phantom was thought appropriate due to the difference in body size from that of a Caucasian male, which was the basis for RCP-AM. The JAEA has developed voxel phantom JM-103 using the average Japanese adult male height and weight (Sato et al. 2010, 2011; Sato and Takahashi 2012, 2017; Manabe et al. 2014), which conformed to the reference voxel phantom RCP-AM defined in ICRP Publication 110 (ICRP 2009). The height and weight of the RCP-AM were 176 cm and 73 kg, respectively, whereas those of the JM-103 were 170 cm and 64 kg.

Concerning the JAEA reports (Sato et al. 2010, 2011; Sato and Takahashi 2012, 2017; Manabe et al. 2014), the ratio of an organ-absorbed dose based on the computational phantoms between RCP-AM and JM-103 by tissue or organ, photon energy (100, 150, 200, 300, 600, and 800 keV), and geometry (AP and ISO) was simulated using the general-purpose radiation transport code PHITS version 2.76, which was developed by the JAEA (Sato et al. 2018). Then, the ratios at energy levels of 119, 207, and 662 keV were interpolated. The selected 14 tissues or organs were the colon, red bone marrow (RBM), esophagus, stomach, liver, gall bladder, spleen, lungs, pancreas, prostate, bladder, kidneys, brain, and heart. Here, the RBM doses for JM-103 and RCP-AM were evaluated by the mass energy absorption coefficient.

The conversion coefficient for JM-103 was estimated by multiplying the above ratio between RCP-AM and JM-103 by the conversion coefficient of organ-absorbed dose per air kerma in ICRP Publication 116 (ICRP 2010) at photon energies of 119, 207, and 662 keV for AP and ISO geometry. Furthermore, the conversion coefficient of an organ-absorbed dose per air kerma under the exposure conditions of NPPs and MA facilities was generated as the weighted mean of the above results, using the proportion values of photon energy and geometry distribution, which was assumed in the 15-Country study (Thierry-Chef et al. 2007).

The uncertainty of the organ-absorbed dose conversion coefficient was considered due to (1) anatomical characteristics (height, organ mass, organ arrangement or shape, etc.), (2) the model used in the simulation code, and (3) statistical errors in the Monte Carlo calculation. However, it was difficult to evaluate the uncertainty quantitatively. In contrast, paragraph 167 of the "Analysis of data variability" in ICRP Publication 74 (ICRP 1996) stated that the coefficients of variation for the calculated organ equivalent dose conversion coefficients were generally less than 2.5% for large organs such as the lungs, liver, and stomach, and less than 1% for organs or tissues distributed throughout the body, such as skin, bone-surface, and bone-marrow. The uncertainty of K_1 was assumed to be 1.050 from $\ln K_1 = 1.96 \times 0.025 = 0.049$, since the conversion coefficients were close to 1 and the upper limit of the coefficients of variation was 2.5%.

B_2 and K_2: Dosimeter response

The bias factor B_2 was defined as the dosimeter reading per air kerma by dosimeter type and nuclear facility type. Table 5, "Dosemeter response and uncertainty by dosemeter type and nuclear facility type," in Furuta et al. (2020a) shows bias B_2 and uncertainty K_2 for GB, EPD, and LB, while Figure 6, "Dosimeter response per air kerma in the work environment experienced by nuclear workers by dosimeter type and nuclear facility type," in Furuta et al. (2020a) shows the B_2 for old FB, multi-element FB, and TLD.

Uncertainty K_2 for old FB, multi-element FB, and TLD was determined according to Table 7, "Dosemeter types used in Japan and the corresponding data from the IARC study," in Furuta et al. (2020a), along with the uncertainties in NPPs and MA facilities that were computed as the weighted average of uncertainties derived from the SD/mean in Table 3, "Response of dosemeters irradiated, on phantom, to three radiation qualities (118, 208 and 662 keV) in AP, rotational and isotropic geometries of exposure," in Thierry-Chef et al. (2002).

Table 1. Transition of photon dose concepts and calibration practices in Japan.

	Period		
Item	Until 1988	1989–2000	2001–present
Compliant ICRP Recommendation	Recommendations; Publication 6 (ICRP 1964)	Recommendations; Publication 26 (ICRP 1977)	1990 Recommendations; Publication 60 (ICRP 1991)
Recorded dose by law	Dose equivalent (rem)	Effective dose equivalent (Sv)	Effective dose (Sv)
Operational quantity	–	Personal dose equivalent $H_p(10)$ (Sv)	Same as the left
Physical quantity	Exposure dose (roentgen)	Fluence or air kerma (Gy)	Same as the left
Phantom defining operational quantity	Free air	ICRU sphere phantom (tissue equivalent substance)	ICRU slab phantom (tissue equivalent substance)
Conversion coefficient of operational quantity per physical quantity	–	Dose equivalent per unit fluence at a depth of 10 mm (Table 6 of Publication 51) (ICRP 1987)	$H_p(10)$ per air kerma (Table A24 of Publication 74) (ICRP 1996)
Phantom used for calibration of personal dosimeter in practice	Free air	Acrylic plate phantom	Aquarium water phantom

B_3 and K_3: Bias factor relating to differences in calibration practice and dose concept

The factor B_3 was a specific bias accounting for any differences in dosimeter calibration concepts. Table 1 summarizes the historical changes in the recorded dose quantities and calibration phantoms. Until 1988, the physical quantity of exposure, expressed in terms of its unit the roentgen (R), was measured by personal dosimeters calibrated in free air; therefore, a dosimeter placed on the human body would indicate a reading slightly higher than the delivered exposure due to the backscattered radiation from the body. Thierry-Chef et al. (2007) stated that the backscatter radiation contributed about 10% of the exposure at the surface.

Table 2, "Conversion coefficients between quantities for cesium, cobalt and radium sources," in Thierry-Chef et al. (2007) shows the factors used to convert the recorded dose to $H_p(10)$. The conversion coefficient of $H_p(10)$ per exposure expressed in R was 1.06/100 (Sv R^{-1}) at the calibration source of cesium (662 keV). However, the dosimeter reading expressed in R was directly read as the dose equivalent (rem) in practice because the rem conversion constant per R was set to 1 by regulation (MOL 1975) and was further converted to $H_p(10)$ in Sv using conversion coefficient of 100 rem = 1 Sv due to the change in the International System of Units (SI). Briefly, when 1 R of radiation was directed to a dosimeter placed on the human body, the dosimeter reading indicated 1.1 R. This reading value included backscatter radiation from the body, which read as 1.1 rem and was further recorded as 1.10/100 Sv. The delivered dose of 1 R was evaluated as $H_p(10)$ of 1.06/100 Sv. Therefore, the bias factor B_3 for the recorded doses until 1988 was defined as the ratio between the recorded dose including backscattered radiation expressed in $H_p(10)$ and the delivered dose in $H_p(10)$: B_3 = (1.10/100) / (1.06/100) = 1/0.96 (Sv Sv^{-1}).

In contrast, personal dosimeters since 1989 have been designed to measure the phantom-related operational quantities, and therefore any corrections for the specific bias in B_3 were unnecessary. Technically speaking, the period since 1989 can be divided into two periods: (1) 1989–2000 when dosimeters were calibrated on an acrylic slab phantom in terms of $H^*(10)$, as a surrogate for H_p (10), and (2) 2001–present when dosimeters were or are calibrated on a water slab phantom in terms of H_p (10). Compared with the roentgen dosimeter era, however, the transitional changes in calibration conditions appear trivial.

Reconstruction of the organ-absorbed dose from 1957 to 2010

With the use of B_1, B_2, and B_3 above, the conversion factor c (Sv Gy^{-1}) defined in eqn (6) was determined as c (p, ft, dt, t), where p was a period (until 1988 or since 1989), ft was nuclear facility type (NPP or MA facility), dt was dosimeter type (old FB, multi-element FB, TLD, GB, EPD, and LB), and t was tissue or organ. The process of reconstructing specific organ-absorbed doses was as follows: (1) the dosimeter type was assigned to the primary personal dosimeter in use at each facility in each year; (2) The annual recorded dose D_R in Sv for each worker exposed at each facility in each year was categorized in relation to the period, nuclear facility type, and dosimeter type was represented as D_R(w, y, f; p, ft, dt), where w was a worker, y was a year between 1957–2010, and f was a facility; and (3) The specific organ-absorbed dose T in Gy for each worker in each year was obtained by dividing the categorized individual annual recorded doses by the corresponding conversion factors and summing them for each worker and year; i.e. T (w, y, t) = Σ_f D_R(w, y, f; p, ft, dt) / c(p, ft, dt, t).

Table 2. Organ-absorbed dose per air kerma (Gy Gy^{-1}) for JM-103.[a]

	Antero-posterior geometry			Isotropic geometry			IB_1		K_1	
	Photon energy (keV)			Photon energy (keV)			(Reciprocal of B_1)			
Tissue or organ	119	207	662	119	207	662	NPP	MA	NPP	MA
Colon	1.38	1.19	1.04	0.70	0.65	0.67	0.84	0.85	1.032	1.029
Red bone marrow (RBM)	1.06	0.92	0.86	0.76	0.68	0.69	0.77	0.78	1.032	1.029
Esophagus	1.11	1.00	0.92	0.64	0.63	0.66	0.78	0.79	1.032	1.029
Stomach	1.48	1.26	1.07	0.71	0.66	0.68	0.86	0.87	1.032	1.029
Liver	1.30	1.13	0.99	0.70	0.65	0.66	0.82	0.82	1.032	1.029
Gall bladder	1.47	1.28	1.09	0.66	0.64	0.66	0.86	0.86	1.032	1.029
Spleen	0.84	0.79	0.78	0.72	0.66	0.67	0.73	0.73	1.032	1.029
Lungs	1.25	1.13	1.03	0.77	0.72	0.74	0.88	0.88	1.032	1.029
Pancreas	1.36	1.18	1.02	0.66	0.59	0.62	0.80	0.81	1.032	1.029
Prostate	1.07	0.98	0.87	0.61	0.58	0.61	0.73	0.74	1.032	1.029
Bladder	1.38	1.18	1.02	0.64	0.61	0.64	0.81	0.82	1.032	1.029
Kidneys	0.92	0.83	0.81	0.66	0.60	0.61	0.70	0.71	1.032	1.029
Brain	0.77	0.76	0.79	0.80	0.77	0.78	0.79	0.79	1.032	1.029
Heart	1.35	1.17	1.02	0.71	0.66	0.69	0.84	0.85	1.032	1.029

[a]Note: (1) RBM was evaluated by the mass energy absorption coefficient. (2) IB_1 was defined as the weighted mean of the above values by energy and geometry using the value of photon energy and geometry distribution. For instance, IB_1 for NPP was computed as:

$IB_{NPP} = \exp[\,0.025 \times 0.5 \times \ln(IB_{119,\,AP}) + 0.075 \times 0.5 \times \ln(IB_{207,\,AP}) + 0.9 \times 0.5 \times \ln(IB_{662,\,AP}) + 0.025 \times 0.5 \times \ln(IB_{119,\,ISO}) + 0.075 \times 0.5 \times \ln(IB_{207,\,ISO}) + 0.9 \times 0.5 \times \ln(IB_{662,\,ISO})\,]$. (3) K_1 for NPP was computed using K = 1.05 as the next:

$K_{NPP} = \exp\{1.96 \times \mathrm{sqrt}[\,0.025 \times 0.5 \times (\ln K/1.96)^2 + 0.075 \times 0.5 \times (\ln K/1.96)^2 + 0.9 \times 0.5 \times (\ln K/1.96)^2 + 0.025 \times 0.5 \times (\ln K/1.96)^2 + 0.075 \times 0.5 \times (\ln K/1.96)^2 + 0.9 \times 0.5 \times (\ln K/1.96)^2\,]\}$.

Reanalysis of cancer mortality for the J-EPISODE

The excess relative risk (ERR) per Gy for mortality from a specific cancer among the J-EPISODE of a male Japanese nuclear worker cohort was estimated in association with a corresponding organ-absorbed dose using a Poisson

regression model, which was applied to cross-classified data for the number of deaths and person-years. Colon dose, the most representative organ-absorbed dose, was applied for an evaluation of death from all solid cancers, and RBM dose for leukemia. The details of the models have been described elsewhere (REA 2015).

RESULTS

B_1 and K_1: Organ-absorbed dose per air kerma for JM-103

Table 2 summarizes the organ-absorbed dose per air kerma, i.e., organ-absorbed dose conversion factor, by tissue or organ for the Japanese male voxel phantom JM-103 (Sato et al. 2010, 2011; Sato and Takahashi 2012, 2017; Manabe et al. 2014). In the case of AP irradiation in all tissues or organs, the lower the energy, the larger the organ-absorbed dose conversion factor. In contrast, in the case of ISO, the difference due to the energy level was small. The organ-absorbed dose conversion factor for ISO was smaller than that for AP for most tissues or organs and energies. The difference in organ-absorbed dose conversion factors between AP and ISO was small in RBM but large in the colon, stomach, liver, lungs, and other organs.

The organ-absorbed dose conversion factor IB_1, the reciprocal of bias B_1, under the average exposure condition was, for instance, 0.84 (Gy Gy^{-1}) in the colon, 0.88 in the lungs, and 0.77 in RBM for NPPs, and 0.85 in the colon, 0.88 in the lungs, and 0.78 in RBM for MA facilities. The values of IB_1 for the lungs and colon, which are located in the anterior surface part of the body, were larger than that of RBM, which is situated deep in the body.

B_2 and K_2: Dosimeter reading per air kerma

Table 3 shows the dosimeter response B_2, i.e., dosimeter reading per air kerma and its uncertainty K_2 by dosimeter type and nuclear facility type. The values of dosimeter responses were between 1.0–1.1 (Sv Gy^{-1}). The dosimeter responses for MA facilities were about 2% larger than those for NPPs. By dosimeter type, the dosimeter responses for FB and LB were relatively large, while those for EPD, GB, and TLD were close to 1.

Table 3. Dosimeter response and uncertainty by dosimeter type and nuclear facility type.[a]

	Dosimeter Response (B_2) (Sv Gy^{-1})		Uncertainty (K_2)	
Dosimeter type	NPP	MA	NPP	MA
Old FB	1.07	1.10	1.034	1.063
Multi-element FB	1.06	1.07	1.026	1.051
TLD	1.02	1.04	1.034	1.048
GB	1.02	1.02	1.011	1.011
EPD	1.00	1.01	1.004	1.003
LB	1.06	1.08	1.037	1.033

[a]Note: (1) Dosimeter response B_2 and uncertainty K_2 for GB, EPD, and LB cited Table 5 of Furuta et al. (2020a). (2) Dosimeter response B_2 for old FB, multi-element FB, and TLD refers to Figure 6 in Furuta et al. (2020a). (3) Uncertainty K_2 for old FB, multi-element FB, and TLD were determined according to Table 7 of Furuta et al. (2020a), along with the uncertainties in NPP or MA that were computed as the weighted average of uncertainties derived from the SD/mean in Table 3 of Thierry-Chef et al. (2002).

Table 4. Bias for the recorded dose until 1988 and its uncertainty.

Period	Quantity	B_3	K_3
Until 1988	Exposure in R[a]	1/0.96 (Sv Sv^{-1})	1.103 (s = 0.05)
Since 1989	$H_p(10)$	1	1 (s = 0)

[a]Despite the relationship of one rem being equivalent to 0.96 R, the value of dosimeter reading in R were in practice recorded in rem as it was until 1988, then converted to Sv due to the change of SI in 1989.

B_3 and K_3: Bias factor for the recorded dose until 1988

Table 4 shows the bias factor B_3 related to calibration practice and dose concept as well as its uncertainty K_3. For the recorded doses in Sv until 1988, which were derived from reading the exposure in R, bias factor B_3 was 1/0.96 (Sv Sv^{-1}) and its uncertainty K_3 was 1.103. For the recorded dose since 1989, B_3 and K_3 were set to 1 for convenience.

Conversion factor from dosimeter reading to organ-absorbed dose

Table 5 shows the values of the first term of exp(m) in eqn (6) by period, dosimeter type, and nuclear facility type for the colon, lungs, and RBM, as well as the associated

Table 5. The first term of eqn (6) of the conversion factor c by period, nuclear facility type, and dosimeter type for the colon, lungs, and RBM, as well as its uncertainty.[a]

	NPPs			MA facilities			Overall uncertainty K	
Dosimeter type	Colon	Lungs	RBM	Colon	Lungs	RBM	NPP	MA
exp(m): the first term of eqn (6) since 1989								
Multi-element FB	1.26	1.20	1.38	1.26	1.22	1.37	1.041	1.059
TLD	1.21	1.16	1.32	1.22	1.18	1.33	1.047	1.056
GB	1.21	1.16	1.32	1.20	1.16	1.31	1.034	1.031
EPD	1.19	1.14	1.30	1.19	1.15	1.29	1.032	1.029
LB	1.26	1.20	1.38	1.27	1.23	1.38	1.049	1.044
exp(m): the first term of eqn (6) until 1988								
Old-FB	1.33	1.27	1.45	1.35	1.30	1.47	1.114	1.126
Multi-element FB	1.31	1.25	1.43	1.31	1.27	1.43	1.112	1.120
TLD	1.26	1.21	1.38	1.27	1.23	1.39	1.114	1.119

[a]Note: (1) The first term of eqn (6) was computed as follows: $\exp(m) = B_1 \times B_2 \times B_3 = (1/IB_1) \times B_2 \times B_3$. (2) By each period, only the dosimeter types used in that period were displayed. (3) Overall uncertainty K was computed using eqn (5).

Table 6. The second term of eqn (6) of the conversion factor c by period, nuclear facility type, and dosimeter type for the colon, lungs, and RBM.[a]

	NPPs			MA facilities		
Dosimeter type	Colon	Lungs	RBM	Colon	Lungs	RBM
exp(s^2/2): the second term of eqn (6) since 1989						
Multi-element FB	1.0004	1.0004	1.0004	1.0004	1.0004	1.0004
TLD	1.0004	1.0004	1.0004	1.0004	1.0004	1.0004
GB	1.0001	1.0001	1.0001	1.0001	1.0001	1.0001
EPD	1.0001	1.0001	1.0001	1.0001	1.0001	1.0001
LB	1.0003	1.0003	1.0003	1.0002	1.0002	1.0002
exp(s^2/2): the second term of eqn (6) until 1988						
Old-FB	1.002	1.002	1.002	1.002	1.002	1.002
Multi-element FB	1.002	1.002	1.002	1.002	1.002	1.002
TLD	1.002	1.002	1.002	1.002	1.002	1.002

[a]Note: The values of exp(s^2/2), the second term of eqn (6) were computed as: $\exp(s^2/2) = \exp\{ [(\ln K_1/1.96)^2 + (\ln K_2/1.96)^2 + (\ln K_3/1.96)^2]/2 \}$.

overall uncertainty K. The values of the second term of exp (s^2/2) in eqn (6), which had a role in contributing the uncertainty of bias to the conversion factor, are shown in Table 6. The values of the second term were negligible, both until 1988 (1.002 for all) and since 1989 (1.0001–1.0004). Therefore, the values of the conversion factor were basically determined by the values of the first term. Table 7 shows the reciprocal of the conversion factor (1/c) by period, nuclear facility type, and dosimeter type for the colon, lungs, and RBM.

The values of the reciprocal of conversion factors were from approximately 0.7 (Gy Sv^{-1}) to 0.9. Fig. 2 shows the reciprocal of conversion factor for EPD at NPPs since 1989 by tissue or organ in order of values. The values were higher in the lungs (0.88), stomach (0.86), and gall bladder (0.86), whereas they were lower in the kidneys (0.70), prostate (0.73), and spleen (0.73).

DISCUSSION

Differences in the 15-Country study and the INWORKS organ-absorbed dose reconstruction methods

This study followed in principle the 15-Country study's organ-absorbed dose reconstruction method described by Thierry-Chef et al. (2007). This method was also used in the INWORKS, as described by Thierry-Chef et al. (2015). Although the INWORKS updated the dosimeter response data, changed the organ-absorbed dose conversion factor from ICRP Publication 74 (ICRP 1996) to Publication 116 (ICRP 2010), and created a time-varying variable to address the neutron exposure condition, the basic framework for converting photon dosimeter readings to organ-absorbed photon doses remained unchanged, even after Thierry-Chef et al. (2015).

Differences in the 15-Country study and the INWORKS facility development times and cohort compositions

Since the 15-Country study and the INWORKS included some facilities that began to operate before the 1950s, much effort was devoted to the comparability of dose concepts and dosimeter calibration practices. In contrast, the Japanese nuclear industry started in the late 1950s; consequently, the concept of exposure dose in R was used from the outset (Table 1). This late start contributed to the simplification of factor B_3 compared with the IARC studies.

Most Japanese nuclear workers worked at NPPs, where half of the reactors were pressurized water reactors (PWRs) and half were boiling water reactors (BWRs). The main source of the photon dose was ^{60}Co. There were no measurable records of neutron exposure from the operating reactor exceeding the detection limit. Moreover, there was no internal exposure to tritium because there was no heavy water reactor (HWR) in Japan.

Additionally, the 15-Country study and the INWORKS included nuclear weapons manufacturing operations in the 1940s and 1950s. Consequently, neutron exposure was a major issue. This study did not encounter this issue because the manufacturing of nuclear weapons has been banned since 1955 under the Japan-US agreement concerning civil uses of atomic energy and related domestic acts in Japan.

Sources of radiation exposure and uncertainties for the J-EPISODE

The organ-absorbed dose reconstruction method described in this study dealt with photon doses only. Fix et al. (1997) and Merwin et al. (2008) discussed in detail the sources of radiation and the possible causes of errors in dosimetry for the IARC Combined Study and Part B of the Energy Employees Compensation Act, respectively. The actions taken in Japan to address these potential problems can

Table 7. Conversion factor from dosimeter reading to organ-absorbed dose by period, nuclear facility type, and dosimeter type for the colon, lungs, and RBM.[a]

	NPPs			MA facilities		
Dosimeter type	Colon	Lungs	RBM	Colon	Lungs	RBM
1/c: reciprocal of conversion factor (Gy Sv^{-1}) since 1989						
Multi-element FB	0.79	0.83	0.73	0.79	0.82	0.73
TLD	0.82	0.86	0.75	0.82	0.85	0.75
GB	0.82	0.86	0.75	0.83	0.86	0.76
EPD	0.84	0.88	0.77	0.84	0.87	0.77
LB	0.79	0.83	0.73	0.79	0.81	0.72
1/c: reciprocal of conversion factor (Gy Sv^{-1}) until 1988						
Old FB	0.75	0.79	0.69	0.74	0.77	0.68
Multi-element FB	0.76	0.80	0.70	0.76	0.79	0.70
TLD	0.79	0.83	0.72	0.78	0.81	0.72

[a]Note: (1) The value c was computed as the product of Tables 5 and 6. (2) The organ-absorbed dose is obtained by multiplying the recorded dose in Sv by (1/c), the reciprocal of the conversion factor.

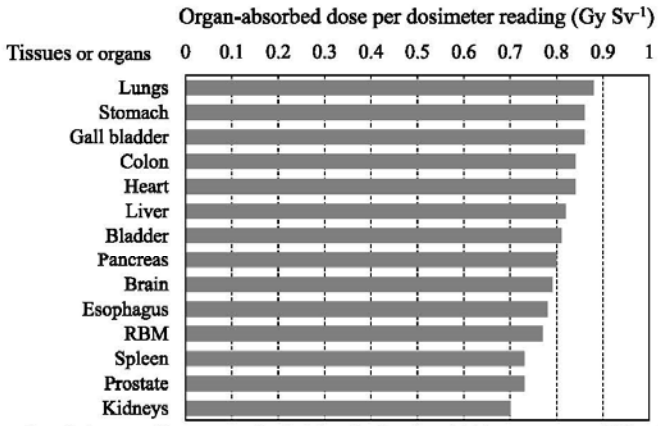

Fig. 2. Conversion factors from dosimeter reading to organ-absorbed dose for the selected 14 tissues or organs (EPD at NPPs since 1989).

be summarized as follows: (1) a medical examination, including a chest x ray, is implemented annually by law, but exposure dose unrecorded; (2) workers are not allowed to enter the controlled area without wearing a personal dosimeter; (3) film badges are to be changed monthly; (4) doses below the detection limit are never recorded as zero, and the RADREC database instead records the number of entries into the controlled area that are below the detection limit; and (5) to address the storage dose for the integrating personal dosimeter, a control dosimeter is to be used to exclude the effect of background radiation.

The study covered the exposure dose resulting from normal work—the work during the operation, periodic inspection, and maintenance in case of NPP—from 1957 to 2010. During the period, neutron exposure was limited only for a few workers, and internal emitter was rare; therefore, the organ-absorbed dose reconstruction and the risk analysis proceeded under the assumption that the recorded dose was predominantly due to photon radiation. In practice, original records of neutron exposure doses and internal doses evaluated in committed doses, if any, are to be kept by each employer. In contrast, by regulation, this information is not recorded in the RADREC database, which includes only the individual annual dose (external dose plus internal dose). After lifting the designation of a nuclear worker, his disaggregated records into external and internal doses are to be sent to the RADREC. However, there is no breakdown of neutron exposure in this document either. Despite thorough investigation and discussion, it is not feasible to identify workers with possible neutron exposure, meaning that it does not make much sense to pursue breakdown into neutron.

During the fabrication of mixed oxide (MOX) fuel containing 20–30% plutonium by weight for the experimental fast breeder reactor Joyo and the prototype reactor Monju at the Nuclear Fuel Cycle Engineering Laboratories (NCL) of JAEA for a certain period, at most 200–300 workers were possibly exposed to neutrons and photons, specifically 60 keV photons from ^{241}Am. However, even for those workers, the contribution of neutron to the effective dose was only about 30% (Yamazaki et al. 2017; Tsujimura et al. 2021). The JAEA-NCL's neutron exposure has existed since the 1980s and has used albedo-type TLD dosimeters. Because the JAEA-NCL has not used a neutron track emulsion type A (NTA) film dosimeter, which has been mentioned by Merwin et al. (2008) and Thierry-Chef et al. (2015) as having a technical defect in that neutrons of about 0.5 MeV or less could not be measured, such problems have not historically occurred in the JAEA.

There have been some cases of internal exposure, but most of them have been minor until 2010. For instance, from the experience of plutonium inhalation accidents in the past decades at the JAEA-NCL, the exposure of one worker in 1993 with an effective dose equivalent of 90 mSv was the largest by far, and the others were trivial, being an average of 0.1 mSv at the MOX plant and 1.5 mSv at the reprocessing plant (Kurihara and Kanai 2011).

After 2010, there were cases of an accident at the TEPCO Fukushima Daiichi Nuclear Power Plant (FDNP) in March 2011, as well as a plutonium contamination accident at the Oarai R&D Institute of JAEA in June 2017 where five workers were internally exposed. In the FDNP accident, there was an internal exposure to ^{131}I and other radionuclides, but the evaluation of internal dose due to emergency work and conversion to an annual organ-absorbed dose is ongoing.

Thus, neutron exposure doses and internal exposure doses, if any, were ignored in organ-absorbed dose reconstruction in the present study.

Differences in body size between Caucasians and Japanese

Regarding the estimation of the organ-absorbed dose per air kerma, the standard Caucasian male phantom RCP-AM was used in the 15-Country study, whereas the average Japanese adult male phantom JM-103 was used in this study. The value of an organ-absorbed dose in the colon and lungs based on JM-103 was about 2% larger than its RCP-AM value (Table 8). Because the Japanese are smaller in body size than Caucasians, their subcutaneous tissue in the abdomen and chest is accordingly thinner. Regarding RBM, in which hematopoietic function is distributed in many tissues, no difference was observed between the two phantoms. At least for adult males, the effect of differences in body size was almost negligible.

Regarding the values of dosimeter response, Furuta et al. (2020a) stated that the results for GB, EPD, and LB in their study were compatible with the results of FB and TLD in the 15-Country study. Therefore, the results of the conversion factor of the present study apply to nuclear worker cohort studies in other countries.

Recently, mesh phantoms have been developed. The voxel phantom can be expressed in mm, whereas the mesh phantom can be described in μm, which allows, for example, an evaluation of the bone surface. However, for the tissues or organs concerned in the present study, mesh phantoms are unlikely to affect the results.

Robustness and generality of the 15-Country study's assumption

Table 2 demonstrates the differences in the values of organ-absorbed dose per air kerma between the AP and ISO for all tissues or organs. This result indicated that the geometry distribution was a strong contributor in estimating the weighted mean for the work environments of NPPs or MA facilities. In such a context, it was crucial that the 15-Country study's assumption of photon energy and geometry distribution was supported by the literature survey results in Japan, as mentioned by Furuta et al. (2020b), indicating the robustness and generality of the assumption.

Reconstruction of the organ-absorbed dose from 1957 to 2010

Table 9 shows the comparison of the cumulative dose between the recorded dose in $H_p(10)$ and a specific organ-absorbed dose reconstructed for the J-EPISODE. While the mean cumulative dose in $H_p(10)$ was 13.9 mSv in 2010, the mean cumulative organ-absorbed dose was 11.0 mGy for the colon, 11.5 mGy for the lungs, and 10.1 mGy for RBM. Neglecting dose-unit differences, organ-absorbed dose values were approximately 0.8 times the recorded doses.

Table 8. Comparison of organ-absorbed dose per air kerma between RCP-AM and JM-103 for the colon, lungs, and RBM (Gy Gy^{-1}).

	NPPs			MA facilities		
Phantom	Colon	Lungs	RBM	Colon	Lungs	RBM
RCP-AM	0.82	0.86	0.77	0.83	0.87	0.78
JM-103	0.84	0.88	0.77	0.85	0.88	0.78

Table 9. Comparison of cumulative dose between $H_p(10)$ and a specific organ-absorbed dose (1957–2010 for 204,103 male workers in the J-EPISODE).

		Organ-absorbed dose (mGy)		
	Recorded dose $H_p(10)$ (mSv)	Colon	Lungs	RBM
Mean cumulative dose in 2010	13.9	11.0	11.5	10.1

This difference of 0.8 between the measured doses and the organ-absorbed doses was fundamentally derived from the estimates of dosimeter responses, the organ-absorbed dose conversion factors used, and the assumption of photon energy distribution and geometry distribution. Of these, the first two were technically determined, so they were thought to be common in all studies. However, the differences in the exposure scenarios of geometry distribution have an impact. The present study, along with the 15-Country study and the INWORKS, assumed that 50% of the exposure dose was in AP and 50% in ISO. In contrast, 50% in AP and 50% in rotational (ROT) geometry was adopted in the IARC Combined Study (Fix et al. 1997). In addition, the MWS recommended using 70% in AP and 30% in ROT if detailed information was not available (Bouville et al. 2015).

As for the results of the INWORKS, the reciprocal of the estimated bias, B_{colon}, B_{lung}, and B_{RBM} for men in Table 1 of Thierry-Chef et al. (2015), corresponded to the ratio of the measured dose to the organ-absorbed dose. The results of the present study were compatible with this finding.

Reanalysis of cancer mortality for the J-EPISODE

For all 204,103 participants in the cohort during the follow-up period 1991–2010, the ERRs Gy^{-1} were estimated for several cancers in association with organ-absorbed doses. Reanalysis results of cancer mortality for the J-EPISODE will be presented separately. Ignoring dose units, the values of the ERRs Gy^{-1} were slightly larger than, or rather about the same as, the corresponding values of the ERRs Sv^{-1} in the previous analysis using $H_p(10)$ (REA 2015), indicating the appropriateness of using the conversion factor from dosimeter readings to organ-absorbed doses for further analysis.

CONCLUSION

The J-EPISODE constructed an organ-absorbed dose conversion factor. Accordingly, the J-EPISODE will use the organ-absorbed dose to estimate the risk of cancer mortality and cancer incidence in the future. A series of companion papers to the present study demonstrated that the 15-Country study's assumption of photon energy and geometry distribution

was robust and general. The dosimeter response data for GB, EPD, and LB were consistent with the 15-Country study and will also be useful for any nuclear worker cohorts. The differences in radiation effects on tissues or organs between the Caucasian and Japanese models were small. Therefore, the conversion factors from dosimeter reading to organ-absorbed dose revealed in the present study can be applied to nuclear worker cohort studies in other countries.

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■■

APPENDIX: PROPERTIES OF LOGNORMAL DISTRIBUTION

When the random variable X follows a lognormal distribution, that is, ln(X) follows a normal distribution with the mean being μ and the standard deviation being σ, i.e. $\ln(X) \sim N(\mu, \sigma^2)$, the mean and median of X can be expressed as follows:

$$\text{Mean}: E(X) = \exp(\mu + \sigma^2/2),$$

$$\text{Median}: \text{Med}(X) = \exp(\mu).$$

When the independent random variables X and Y follow a lognormal distribution, i.e. $\ln(X) \sim N(\mu_X, \sigma_X^2)$ and $\ln(Y) \sim N(\mu_Y, \sigma_Y^2)$, the product XY also follows a lognormal distribution because the normal distribution has reproducibility:

$$\ln(XY) = \ln(X) + \ln(Y) \sim N(\mu_X + \mu_Y, \sigma_X^2 + \sigma_Y^2).$$

■■

２．３　外部専門家との意見交換会

令和３年度 ICRP 調査・研究連絡委員会「外部専門家との意見交換会」

開催日時:　令和３年 12 月 20 日(月)　14 時 00 分～16 時 40 分
開催形式:　ZOOM ウェビナーによる WEB セミナー
テ ー マ:　放射線作業者の疫学調査に期待される知見と課題
主　　催:　公益財団法人放射線影響協会
参 加 費:　無料

ICRP は 2007 年基本勧告において、職業被ばく集団の疫学調査の重要性について述べています。我が国では低線量・低線量率における健康影響の知見を得ることを目的として、原子力施設の放射線業務従事者を対象とした放射線疫学調査を実施しております。これらの疫学調査について、現状と課題に関する理解を深めることを目的とし本意見交換会を開催いたします。

プログラム

（敬称略）

14:00 ～ 14:05 開会の辞　放射線影響協会
14:05 ～ 15:05 意見交換会第1部　進行　放射線影響協会
14:05 ～ 14:20　我が国における放射線の健康影響にかかわる疫学調査について
　吉永 信治(広島大学原爆放射線医科学研究所 教授)
14:20 ～ 14:35　J-EPISODE における線量評価　～臓器線量の構築～
　古田 裕繁(放射線影響協会放射線疫学調査ｾﾝﾀｰ 統計担当部長)
14:35 ～ 14:50　J-EPISODE における健康影響の解析　～交絡因子の調整～
　工藤 伸一(放射線影響協会放射線疫学調査ｾﾝﾀｰ 統計課長)
14:50 ～ 15:05　東京電力福島第一原子力発電所 緊急作業従事者の疫学調査研究
　大久保 利晃((独)労働者健康安全機構労働安全衛生総合研究所
　労働者放射線障害防止研究ｾﾝﾀｰ長)
15:05 ～ 15:15 休憩
15:15 ～ 16:15 意見交換会第２部 パネル討論　モデレーター 甲斐 倫明(ICRP 主委員会委員)
討論のポイント・ 低線量・低線量率の疫学調査における検出力
・ 生活習慣の影響の評価
・ 調査結果の解釈
パネラー:　ご講演者(吉永信治 古田裕繁 工藤伸一 大久保利晃)に加え
小笹晃太郎・島田義也(ICRP C1委員) 細野眞(C3 委員)
三枝 新(放射線影響協会放射線疫学調査ｾﾝﾀｰ長)の８名
16:15 ～ 16:35 聴衆との質疑応答　モデレーター 甲斐 倫明
16:35 ～ 16:40 閉会の辞　放射線影響協会

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