日中笹川医学奨学金制度(学位取得コース)評価書
課程博士：指導教官用

第 41 期　研究者番号：G4109　作成日：2021 年 3 月 1 日

Supported by 日本財団 THE NIPPON FOUNDATION

氏　名	張　含鳳	ZHANG HANFENG	性別	F	生年月日　1986.07.27
所属機関（役職）	四川省腫瘤医院放療病区（主管護師）				
研究先（指導教官）	広島大学大学院医系科学研究科保健学分野（宮下 美香教授）				
研究テーマ	中国の生殖年齢にある男性がん患者の妊孕性温存をめざした支援プログラムの効果 Acutual situation of fertility preservation to the reproductive-aged male cancer patients in China				
専攻種別	☐論文博士	☑課程博士			

研究者評価（指導教官記入欄）

成績状況	(優)　良　可　不可 ~~学~~業成績係数=	取得単位数 21／22
学生本人が行った研究の概要	中国における医療専門職者および男性がん患者の妊孕性温存に関する知識、態度、行動を明らかにすることを目的とし、男性がん患者 15 名、看護師 8 名、医師 8 名を対象とし、面接調査を実施した。結果、看護師の知識が不十分であるため患者へ推奨される実践がなされていないこと、看護師は教育を受けることへの希望を有していることがわかった。医師、患者の面接調査結果については、現在分析中である。なお、本研究に先立ち、がん患者の妊孕性温存に関する医療者への教育プログラムについて系統的文献検討を行い、教育プログラムの有効性が確認されたが、教育プログラムの評価ツールの開発、評価するための質の高い無作為化比較試験の実施が課題であることが明らかとなった。	
総合評価	【良かった点】 常に精力的に研究に取り組み、博士論文に関連する論文（系統的文献検討）が英文誌に掲載された。調査は新型コロナウイルス感染症の流行に伴い、思うように進まなかったが、予定の人数のインタビューを終えることができた。分析は順調に進んでいる。 【改善すべき点】 特にございません。 【今後の展望】 面接調査を予定どおり実施できなかったため、全国調査を実施することができなかった。2021 年度の学位取得を目指し、面接調査の結果を論文化、投稿することを検討する。	
学位取得見込	現時点では、2022 年 3 月を予定している。	

評価者（指導教官名）　宮下　美香　㊞

日中笹川医学奨学金制度(学位取得コース)報告書
研究者用

第41期　研究者番号：　G4109　作成日：2021年3月1日

氏名	Zhang Hanfeng	張　含鳳	性別	F	生年月日　1986. 07. 27
所属機関(役職)	四川省腫瘤医院放療病区（主管護師）				
研究先（指導教官）	広島大学大学院医系科学研究科　保健学分野（宮下 美香教授）				
研究テーマ	中国の生殖年齢にある男性がん患者の妊孕性温存をめざした支援サービス:患者と医療専門職者の視点からの定性研究 The oncofertility service for male cancer patients in China: A qualitative study from the perspectives of patients and healthcare providers				
専攻種別	論文博士	☐	課程博士	☑	

１．研究概要（1）

1）目的（Goal）

The survival rates of patients with cancer have increased significantly with improvements in detection and treatments, allowing greater attention to their long-term quality of life. The ability to produce children is widely considered to be important for cancer survivors of reproductive age. The fertility of cancer patients can be affected by various factors, including age, cancer type, and cancer treatment. For men, an adverse outcome of cancer treatment may be temporary or permanent azoospermia. The American Society of Clinical Oncology, and the European Society for Medical Oncology have recommended the cryopreservation of sperm in men as standard strategies for fertility preservation (FP). In fact, many cancer survivors report a strong desire to maintain fertility and prefer to have their own biologic children. Cancer survivors who have preserved their fertility are better ability to cope with their cancer, whereas patients without hope of a child often experience anxiety, depression, and grief. In traditional Chinese culture, continuing the family line is very important. The unmarried infertile woman may remain single, while a married couple is more prone to an unstable marriage and divorce. Hence, in China patients who are infertile experience greater social pressures than do their counterparts in Western countries. The Chinese government approved a new child policy in 2015, in which each couple is allowed to have two children. This new policy provides every Chinese person, including cancer patients, permission to have another baby. The concerns of Chinese cancer patients who risk damage to their fertility should be given greater attention. Therefore, the main aim of this study is to explore the knowledge, attitude and practice of Chinese healthcare providers in providing oncofertility service for male cancer patients, as well as identify the current knowledge, attitude and behavior of FP in male cancer patients with childbearing age.

2）戦略（Approach）

The semi-structured interviews were conducted in this study. Research Ethics Board approval was received from the Hiroshima University and the Sichuan Cancer Hospital.

3）材料と方法（Materials and methods）

3.1 Study participants and sample

The male cancer patients with child-bearing age and healthcare providers in Sichuan Cancer Hospital were invited to participate in this study.

3.1.1 Study population-male patients with cancer

Inclusion criteria of this study are (1) male patients in age group of 18 to 45 years, (2) patients with nasopharyngeal carcinoma, leukemia, malignant lymphoma received chemotherapy or brain cancer patients received radiotherapy, (3) patients with rectal cancer, bladder cancer, testicular cancer and prostate cancer received surgery or chemotherapy or radiation therapy, (4) patients with stage Ⅰ~Ⅲ, (5) patients are undergoing cancer treatments or have finished treatments within one year, (6) patients can read and write in Chinese, (7) inform consent was received from patients. Exclusion criteria of this study are (1) participants received cancer treatments in other hospitals and could not recall their treatments clearly, (2) patients were considered unsuitable to take part in this study because of health problems or mental disorders.

3.1.2 Study population-health care professionals

Inclusion criteria consisted of: (1) a specialization in oncology, oncology nursing, reproductive endocrinology, or andrology; (2) a medical or nursing degree; (3) routine clinical contact with cancer patients or survivors; and (4) working experience is more than one year. The healthcare providers with less than one year of work experience or who are unwilling to participate in the study are excluded.

3.1.3 Sample

Purposive sampling was used to increase representativeness of the study. Fifteen male patients with cancer and thirty-one healthcare providers (8 oncologists, 18 oncology nurses, and 5 fertility specialists) were recruited in this study.

3.2 Methods

3.2.1 Participants recruitment

The male cancer patients were included by using posters which were put in the outpatient and inpatient building. Participants who interest in participating in this study contacted us by telephone or email. In addition, the health care professionals were recruited with the help of the head of Department of Nursing and the Clinical Directors. Then we provided the participants with detailed information about the study, confirm eligibility, and scheduled the interview. Interviews were finished in a separate office in the hospital. Before interviews, participant information leaflet was provided and informed.

１．研究概要（2）

consent was taken from interviewee. After providing consent, filling out participant information leaflet, a semi-structured interview guide was used during the audio-recorded, one-on-one interview. The interview each lasted 10-40 minutes, and all participants speak Chinese.

3.2.2 Data Management and Analysis

Demographic data were summarized using descriptive statistics. Recordings were transcribed verbatim from audio recordings. Each researcher independently coded one transcript to test for consistency and compared across the others. Once consensus was reached, data were coded by one study team member, using NVivo 12. Inductive thematic analysis was employed to derive common themes, following the study framework. Discrepancies in opinion regarding themes were resolved using group discussion to ensure that the findings logically flowed from the raw coded data. To analyze the data, following steps are followed:1. Transcription, proof-reading of interview and re-reading to acquire understanding of experiences; 2. Line by line reading to identify broad area of phenomena being captured; 3. Statements assigned meanings to enable recognition of intricate details pertaining to phenomena; 4. Codes grouped into cluster of themes and categories; 5. Findings integrated into exhaustive description of phenomena and provided to supervisors for review; 6. Feedback of supervisors incorporated to reflect universal features of phenomena.

4）実験結果（Results）

4.1 the results of interview with oncology nurses

Summary of Themes（nurses）

Category	Subcategory	Theme
Knowledge of FP	Assessment	Educational pattern
		Access to information
	Training desire	Systematic training content
		Practical training
Practice engagement	Counseling	Awareness
		Comfortable level of discussion
	Collaboration	Nurse-doctor collaboration
		Nurse-fertility specialist communication
	Barriers	Ignorance
		Insufficient knowledge
		Unclear responsibility
		Feedback of patients
		Culture and personality
		Relationship between patients and nurses
Attitude towards FP	Negative issues	Unavailability of FP guidelines
		potential risk
	Positive trends	Awareness of importance of FP
		Policy proposal and suggestions

4.2 the results of interview with other healthcare providers and cancer patients (ongoing)

5）考察（Discussion）

Lack of knowledge and access to information of FP among oncology nurses was one of the most prominent findings. Therefore, most of nurses did not play the role of routinely informing male patients as recommended by the ICCN guidelines. Nurses have a positive attitude toward FP, but they are preoccupied with concern of their own professional competence and have strong training desire about FP. In addition, culture, personality, unclear responsibility and lack of guidelines hindered their practices regarding FP. It is highly recommended to introduce new systematic training courses for oncology nurses to improve their FP application. Nurses agree that the policy, regulations and guidelines of FP should take the lead for improving the oncofertility services for male cancer patients of reproductive age.

6）参考文献（References）

1) Griggs JJ, Sorbero ME, Mallinger JB, Quinn M, Waterman M, Brooks B et al (2007) Vitality, mental health, and satisfaction with information after breast cancer. Patient Educ Couns 66:58-66.

2) Duffy C, Allen S (2009) Medical and psychosocial aspects of fertility after cancer. Cancer J 15:27-33.

3) Ajala T, Rafi J, Larsen-Disney P, Howell R (2010) Fertility preservation for cancer patients: a review. Obstet Gynecol Int 2010:160386.

4) Loren AW, Mangu PB, Beck LN, Brennan L, Magdalinski AJ, Partridge AH, Quinn G, Wallace WH, Oktay K (2013) Fertility preservation for patients with cancer: American Society of Clinical Oncology clinical practice guideline update. J Clin Oncol 31:2500-2510.

5) Peccatori FA, Azim HA Jr, Orecchia R, Hoekstra HJ, Pavlidis N, Kesic Vetal (2013) Cancer, pregnancy and fertility: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. Ann Oncol 24 (Suppl 6):vi160-vi170.

6) Saito K, Suzuki K, Iwasaki A, Yumura Y, Kubota Y (2005) Sperm cryopreservation before cancer chemotherapy helps in the emotional battle against cancer. Cancer. 104:521-524.

7) Rosen A, Rodriguez-Wallberg KA, Rosenzweig L (2009) Psychosocial distress in young cancer survivors. Semin Oncol Nurs 25:268-277.

8) Lambertini M, Del Mastro L, Pescio MC, Andersen CY, Azim HA Jr, Peccatori FA et al (2016) Cancer and fertility preservation:international recommendations from an expert meeting. BMC Med 14(1):1.

9) Urech C, Ehrbar V, Boivin J, Müller M, Alder J, Zanetti Dällenbach R, Rochlitz C, Tschudin S (2018) Knowledge about and attitude towards fertility preservation in young female cancer patients: a cross-sectional online survey. Hum Fertil (Camb) 21:45-51.

10) Sallem A, Shore J, Ray-Coquard I, Ferreux L, Bourdon M, Maignien C, Patrat C, Wolf JP (2018) Fertility preservation in women with cancer: a national study about French oncologists awareness, experience, and feelings. J. Assist. Reprod. Genet 35: 1843-1850.

2. 執筆論文Publication of thesis※記載した論文を添付してください。Attach all of the papers listed below.

<table>
<tr><td>論文名 1
Title</td><td colspan="7">The Educational Program for Healthcare Providers Regarding Fertility Preservation for Cancer Patients: a Systematic Review</td></tr>
<tr><td rowspan="2">掲載誌名
Published journal</td><td colspan="7">Journal of Cancer Education</td></tr>
<tr><td>2020 年 10 月</td><td>15 巻（号）</td><td colspan="2">頁 ～ 頁</td><td>言語
Language</td><td colspan="2">English</td></tr>
<tr><td>第 1 著者名
First author</td><td>Han-feng Zhang</td><td>第 2 著者名
Second author</td><td colspan="2">Qing-hua Jiang</td><td>第 3 著者名
Third author</td><td colspan="2">Gui-yu Huang</td></tr>
<tr><td>その他著者名
Other authors</td><td colspan="7">Jun Kako, Kohei Kajiwara, Jian-xia Lyu, Mika Miyashita</td></tr>
<tr><td>論文名 2
Title</td><td colspan="7">Research progress of fertility preservation service for patients with malignant tumor</td></tr>
<tr><td rowspan="2">掲載誌名
Published journal</td><td colspan="7">Journal of Nursing Science</td></tr>
<tr><td>2020 年 5 月</td><td>35 巻（号）</td><td colspan="2">107 頁 ～ 111 頁</td><td>言語
Language</td><td colspan="2">Chinese</td></tr>
<tr><td>第 1 著者名
First author</td><td>Han-feng Zhang</td><td>第 2 著者名
Second author</td><td colspan="2">Gui-yu Huang</td><td>第 3 著者名
Third author</td><td colspan="2">Ying-hong Fang</td></tr>
<tr><td>その他著者名
Other authors</td><td colspan="7">Li-feng Ruan, Hong-fang Bai, Jian Zhang, Qing-hua Jiang</td></tr>
<tr><td>論文名 3
Title</td><td colspan="7">Importance and safety of autologous sperm cryopreservation for fertility preservation in young male patients with cancer</td></tr>
<tr><td rowspan="2">掲載誌名
Published journal</td><td colspan="7">Medicine</td></tr>
<tr><td>2020 年 4 月</td><td>99 巻（号）</td><td colspan="2">1 頁 ～ 8 頁</td><td>言語
Language</td><td colspan="2">English</td></tr>
<tr><td>第 1 著者名
First author</td><td>Yin-feng Li</td><td>第 2 著者名
Second author</td><td colspan="2">Jian Zhang</td><td>第 3 著者名
Third author</td><td colspan="2">Han-feng Zhang</td></tr>
<tr><td>その他著者名
Other authors</td><td colspan="7">Bo Liu, Guo-rong Wang, Mao-qiu Cao, Ben-cui Fu, Hui Li, Qing-hua Jiang, Lin Yu, Yang Xian, Bi-zhen Su, Xiao-hui Jiang</td></tr>
<tr><td>論文名 4
Title</td><td colspan="7"></td></tr>
<tr><td rowspan="2">掲載誌名
Published journal</td><td colspan="7"></td></tr>
<tr><td>年 月</td><td>巻（号）</td><td colspan="2">頁 ～ 頁</td><td>言語
Language</td><td colspan="2"></td></tr>
<tr><td>第 1 著者名
First author</td><td></td><td>第 2 著者名
Second author</td><td colspan="2"></td><td>第 3 著者名
Third author</td><td colspan="2"></td></tr>
<tr><td>その他著者名
Other authors</td><td colspan="7"></td></tr>
<tr><td>論文名 5
Title</td><td colspan="7"></td></tr>
<tr><td rowspan="2">掲載誌名
Published journal</td><td colspan="7"></td></tr>
<tr><td>年 月</td><td>巻（号）</td><td colspan="2">頁 ～ 頁</td><td>言語
Language</td><td colspan="2"></td></tr>
<tr><td>第 1 著者名
First author</td><td></td><td>第 2 著者名
Second author</td><td colspan="2"></td><td>第 3 著者名
Third author</td><td colspan="2"></td></tr>
<tr><td>その他著者名
Other authors</td><td colspan="7"></td></tr>
</table>

3．学会発表　Conference presentation　※筆頭演者として総会・国際学会を含む主な学会で発表したものを記載してください。

※Describe your presentation as the principal presenter in major academic meetings including general meetings or international meetings.

学会名 Conference	Oncology Nursing Society (ONS) 44th Annual Congress			
演　題 Topic	Level of knowledge and needs on fertility preservation in reproductive-aged male patients with cancer			
開催日 date	2019　年　4　月　11　日	開催地 venue	Anaheim, USA	
形式 method	☐ 口頭発表 Oral ☑ ポスター発表Poster	言語 Language	☐ 日本語 ☑ 英語 ☐ 中国語	
共同演者名 Co-presenter	No			
学会名 Conference	Oncology Nursing Society (ONS) 45th Annual Congress			
演　題 Topic	Current status and influencing factors of four-dimensional comfort in cervical cancer patients with painless interstitial brachytherapy			
開催日 date	2020　年　4　月　29　日	開催地 venue	San Antonio, USA (online)	
形式 method	☐ 口頭発表 Oral ☑ ポスター発表Poster	言語 Language	☐ 日本語 ☑ 英語 ☐ 中国語	
共同演者名 Co-presenter	No			
学会名 Conference				
演　題 Topic				
開催日 date	年　月　日	開催地 venue		
形式 method	☐ 口頭発表 Oral ☐ ポスター発表Poster	言語 Language	☐ 日本語 ☐ 英語 ☐ 中国語	
共同演者名 Co-presenter				
学会名 Conference				
演　題 Topic				
開催日 date	年　月　日	開催地 venue		
形式 method	☐ 口頭発表 Oral ☐ ポスター発表Poster	言語 Language	☐ 日本語 ☐ 英語 ☐ 中国語	
共同演者名 Co-presenter				

4．受賞（研究業績 Award (Research achievement)

名　称 Award name	Award of Young Talent			
	国名 Country	China	受賞年 Year of	2020　年　9　月
名　称 Award name	Medical Science and Technology Award of Sichuan Province			
	国名 Country	China	受賞年 Year of	2021　年　2　月

5. 本研究テーマに関わる他の研究助成金受給 Other research grants concerned with your resarch theme

受給実績 R ecept record	□ 有　■ 無
助成機関 名称 Funding agency	
助成金名称 Grant name	
受給期間 Supported period	年　月 ～ 年　月
受給額 Amount received	円
受給実績 R eceip record	□ 有　■ 無
助成機関 名称 Funding agency	
助成金名称 Grant name	
受給期間 Supported period	年　月 ～ 年　月
受給額 Amount received	円

6. 他の奨学金受給 Another awarded scholarship

受給実績 Receipt record	□ 有　■ 無
助成機関名称 Funding agency	
奨学金名称 Scholarship name	
受給期間 Supported period	年　月 ～ 年　月
受給額 Amount received	円

7. 研究活動に関する報道発表 Press release concerned with your research activities

※記載した記事を添付してください。Attach a copy of the article described below

報道発表 Press release	□ 有　■ 無	発表年月日 Date of release	
発表機関 Released medium			
発表形式 R elese method	・新聞　・雑誌　・Web site　・記者発表　・その他（　　）		
発表タイトル Released title			

8. 本研究テーマに関する特許出願予定 Patent application concerned with your research theme

出願予定 Scheduled	□ 有　■ 無	出願国 Application	
出願内容（概要） Application contents			

9. その他 Others

指導責任者（署名）　宮下美香

Journal of Cancer Education
https://doi.org/10.1007/s13187-020-01890-3

The Educational Program for Healthcare Providers Regarding Fertility Preservation for Cancer Patients: a Systematic Review

Han-feng Zhang [1,2] · Qing-hua Jiang [2] · Gui-yu Huang [2] · Jun Kako [3] · Kohei Kajiwara [4] · Jian-xia Lyu [2] · Mika Miyashita [1]

Accepted: 30 September 2020

Abstract

The emerging discipline of oncofertility advocates for the timely provision of fertility preservation (FP) to all cancer patients of childbearing age by healthcare providers. A lack of practice due to limited FP-related knowledge was found among healthcare providers. A systematic review was undertaken on the educational programs on FP for healthcare providers. An initial search was performed in MEDLINE, PsycINFO, CINAHL, Web of Science, PubMed, and Scopus databases in October 2019. This review was guided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement. Among the 160 articles that were identified, five relevant articles published between 2009 and 2019 were reviewed. Of the five studies, three were quantitative nonrandomized studies, one was a randomized controlled trial, and one was a qualitative study. Three programs were relevant to oncology nurses, one was relevant to social workers as well as nurses, and one was relevant to oncology fellows and residents. The four programs significantly increased healthcare providers' knowledge about FP, but clinical practice was only improved in the Educating Nurses about Reproductive Issues in Cancer Healthcare program ($P < 0.01$). Nevertheless, most of the studies used a self-made questionnaire or tool to assess the effects of the training programs. The educational programs improved the FP-related knowledge of healthcare providers but lacked the high-quality randomized controlled trials needed to provide robust evidence on the effectiveness of training programs using standard tools. More training projects should be developed based on learning theories or models to improve oncofertility care in clinical practice.

Keywords Cancer · Education · Fertility preservation · Health personnel · Oncology

Background

The survival rates of patients with cancer have increased significantly with improvements in detection and treatment, allowing greater attention to their long-term quality of life. The ability to produce children is widely considered important for cancer patients of reproductive age [1]. The fertility of cancer patients can be affected by various factors, including age, cancer type, and cancer treatment [2, 3]. Although it is difficult to precisely predict the chance of infertility for cancer patients, some anti-treatments generally yield infertility rates of 80% or more [4].

Fertility is one of the greatest concerns for cancer patients [5]. Many cancer survivors report a strong desire to maintain fertility and prefer to have their own biologic children [6, 7]. Cancer patients who have preserved their fertility are better able to cope with their cancer [8], whereas patients without hope of producing a child often experience anxiety, depression, and grief [9, 10].

Given the importance of fertility preservation (FP), international guidelines recommend that physicians should discuss fertility issues with all cancer patients of childbearing age as early as possible even if the patients have poor prognoses or advanced disease [11, 12]. Despite these guidelines, many studies have shown that physician referral for FP for cancer patients is still unsatisfactory [13, 14]. A recent review showed that cancer patients lack FP information and are not informed about

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s13187-020-01890-3) contains supplementary material, which is available to authorized users.

✉ Mika Miyashita
mikamiya@hiroshima-u.ac.jp

1 Department of Gerontological and Oncology Nursing, Graduate School of Biomedical and Health Sciences, Hiroshima University, Hiroshima, Japan

2 Department of Radiation Oncology, Sichuan Cancer Hospital & Institute, Sichuan Cancer Center, Radiation Oncology Key Laboratory of Sichuan Province, School of Medicine, University of Electronic Science and Technology of China, Chengdu, China

3 College of Nursing Art and Science, University of Hyogo, Hyogo, Japan

4 Japanese Red Cross Kyushu International College of Nursing, Fukuoka, Japan

Published online: 15 October 2020

FP options regularly [15]. Although oncologists ideally would conduct FP discussions with all patients, it is unrealistic because of many barriers, such as lack of knowledge of FP, perceived lack of time to discuss fertility issues, and prioritizing cancer treatment [16–18]. The percentages of oncologists who discuss fertility issues in Saudi Arabia, Japan, and the UK were reported to be 42%, 42.7%, and 97%, respectively [19–21]. In 2013, the American Society of Clinical Oncology (ASCO) extended the responsibility for discussion and referral about FP for cancer patients of childbearing age beyond physicians to include nurses and other allied healthcare providers [1]. Many authors also suggested that oncology nurses and social workers may be suitable to be involved in the discussion and referral process about FP [22]. However, oncology nurses and social workers reported their knowledge was insufficient to accomplish these tasks [23, 24].

Fortunately, the need for healthcare providers to receive more education in FP has been increasingly recognized. In 2005, Fertile Hope launched their Centers of Excellence (COE) program (FHCOE program), which continued until Fertile Hope's acquisition by LIVESTRONG in 2009, which provided access to medical professionals with educational resources to improve patient-provider communication, and tools to implement systematic change that can lead to better care [25]. Moreover, bundled interventions including delivery of targeted education sessions for medical and senior nursing clinicians were introduced during 2015 across the Youth Cancer Service in Australia [26]. Despite the increased awareness of the need to educate oncology healthcare professionals, a comprehensive evaluation of the effects of training is still lacking.

Better insight into the features and effects of FP educational programs is needed to assist healthcare providers, educators, and managers in oncofertility care around the world by selecting and implementing programs based on available evidence. Therefore, we systematically reviewed studies to evaluate the educational programs on FP for oncology healthcare providers.

Methods

This systematic review was conducted in accordance with the guidelines for performing and reporting systematic reviews and meta-analyses [27]. The protocol of this review is accessible on the International Prospective Register of Systematic Reviews (PROSPERO) website (registration number CRD42020154081).

Literature Search

MEDLINE, PsycINFO, CINAHL, Web of Science, PubMed, and Scopus databases were used to find studies published between January 2000 and October 2019. Search terms were tailored to individual databases in order to take an inclusive approach (Table 1). References of the selected articles were manually screened to identify additional relevant studies. In addition, study authors were contacted to identify additional studies and some relevant websites were searched (i.e., Oncology Nursing Society, International Society for Fertility Preservation, LIVESTRONG, the Oncofertility Consortium, Memorial Sloan Kettering Cancer Center, Moffitt Cancer Center, and Northwestern Medicine). In order to get the full gray literature, trial registers, such as clinical trials and PROSPERO, were also checked.

Study Selection

All research results were exported into Endnote X7.1 to deduplicate results. All titles and abstracts were screened by the primary author. Two reviewers reviewed the remaining studies to determine eligibility for inclusion independently. Discrepancies about inclusion were resolved by discussion, or with a third reviewer. Studies were included if they (1) tested an educational program or training for FP; (2) were for healthcare providers who care for cancer patients (i.e., oncologists, nurses, social workers); (3) reported one or more educational outcome effect as classified by the Kirkpatrick hierarchical model, such as learner knowledge, attitude, skills, behavioral changes, and satisfaction [28]; and (4) were described in a published article in English. Articles that did not present data on outcomes (e.g., a review, meeting abstract) were excluded.

Data Extraction and Analysis

A standard data entry form was used to extract data from the included articles by two reviewers. Information about authors, year of publication, country, objectives, methods, sample size, programs performed, measurement of program, details of program, results, and conclusion was analyzed. Studies were listed chronologically by publication date. For some information not mentioned in the article, we contacted authors to clarify the contents by e-mail and determined the risk of bias in the individual studies. Disagreement about the process of data extraction among the researchers was resolved through consensus. Data synthesis was based on content and was categorized as quantitative, qualitative, and mixed-methods data. A narrative synthesis of the findings from the included studies was provided.

Quality Assessment

The quality of each article was assessed by two investigators using the latest version of the Mixed Methods Appraisal Tool (MMAT) [29]. The MMAT allows for simultaneous evaluation

Table 1 Search terms utilized across all electronic databases

Cancer		Fertility		Healthcare providers		Educational program
Neoplasm* or oncology or tumor or malignancy or carcinoma or cancer	AND	Fertility or infertility or oncofertility or cryopreservation or preservation or conservation or sperm bank* or storage or reproductive technique*	AND	Healthcare provider* or health care provider* or health professional* or health personnel* or nurse* or physician* or doctor* or oncologist* or clinician* or fellow* or social worker*	AND	Education* or educate or program* or service* or intervention* or development or learning or training* or treatment or skill* or competence* or knowledge or support

of all empirical literature (i.e., qualitative, quantitative, and mixed-methods studies) [30]. The content validity of this tool has been verified [31]. Quality assessment was completed independently by two researchers, and the quality score ranged from meeting none of the five criteria (zero) to meeting all five criteria (five). Scores were then compared and discussed until a consensus was reached. The screening and exclusion process were presented using an adapted Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flowchart (see Fig. 1).

Results

Search Results

The literature search resulted in 160 potential articles. Six papers were manually retrieved. Sixty-one records were screened by title and abstract. Thirty-three full-text articles were retrieved and reviewed, of which 28 were excluded. The reasons for exclusion included are as follows: (1) a systematic review ($n = 1$); (2) the title and abstract were published in English, but the text of the article was in Spanish ($n = 1$); (3) a program review without data ($n = 3$); (4) a meeting abstract ($n = 15$); and (5) the text of article was not relevant ($n = 8$) (e.g., survey of the need for education; reliability and validity test of educational programs; survey of usage of education materials).

Study Characteristics

The five articles reported on four different educational programs (Educating Nurses about Reproductive Issues in Cancer Healthcare (ENRICH), non-physician training, Fex-Talk, and Banking on Fatherhood (BOF) educational tool) published between 2009 and 2019 [32–36]. The majority of studies were conducted in the USA ($n = 3$), and the other two studies were conducted in Sweden and Japan. Of the five studies, three were quantitative nonrandomized studies, one was a randomized controlled trial, and one was a qualitative study. The numbers of participants ranged from 77 to 233 in the quantitative nonrandomized studies; however, the randomized controlled trial had a small sample with only 19 participants (Table 2).

Quality Critical Appraisal

The methodological quality of the studies ranged from 2 (low) to 5 (high). The lowest MMAT score was the randomized controlled trial, which did not provide detailed information about the randomization methods, baseline comparison, and application of blind method. The score of the three quantitative nonrandomized studies was 4, a high MMAT score; however, these studies had the same limitation of not considering confounders in the design and analysis parts. The qualitative study had the highest quality with a score of 5 (Table 2).

Characteristics of the Educational Programs

Of the four programs, the ENRICH and Fex-Talk programs were provided for nurses and the BOF educational tool was for oncology fellows and residents, and the non-physician training program was conducted for nurses and social workers.

In regard to program design, only the ENRICH program was a medium-term training project that consisted of 60–90-min sessions over 8 weeks, two programs were short term and lasted 2–4 h, and one program did not report the time allocated (Table 3). Three programs were performed via lecture with a web-based version or face-to-face format. Two programs used multimedia teaching methods, which consisted of videos and animation. Case studies, role-play, and various assignments were also used in these programs (Table 3).

Four programs addressed a range of topics related to training. The most common topics mentioned in the programs were infertility as a potential risk of cancer treatment and FP options. The ENRICH and Fex-Talk programs provided

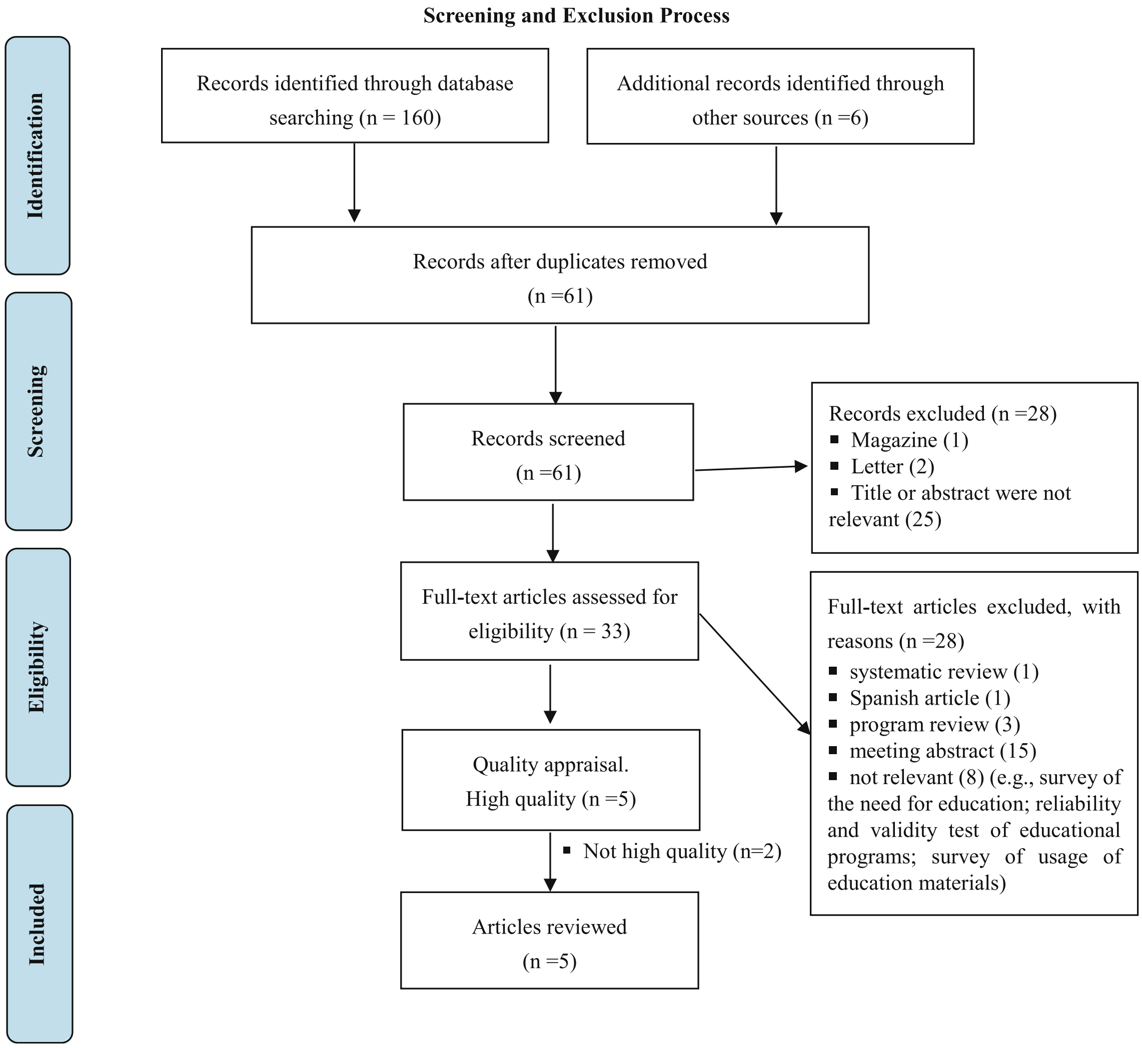

Fig. 1 Screening and exclusion process

communication strategies for participants. In addition, psychosocial support was also taught in the ENRICH and non-physician educational programs. A checklist of topics to discuss with patients was provided in the BOF program, while alternative family building options as well as some ethical and legal issues regarding the FP were included in the ENRICH program (Table 3).

For the program evaluation, in addition to the use of true/false choice tests (BOF educational tool), more than half of the studies used a self-made questionnaire to assess pre-post effects on the respondents' knowledge level and used a self-appraisal tool to rate behavior, practice, and institutional change in quantitative studies (Table 2), potentially introducing response bias.

Moreover, three quantitative studies completed a 6-month follow-up survey after the education program, but only 54%, 59.7%, and 70% of participants returned them, which may also create a risk of response bias.

Changes in Knowledge and Confidence

Among these five studies, four quantitative studies reported statistically significant overall knowledge improvements ($P < 0.01$). The BOF educational tool improved knowledge about cancer-related infertility and sperm banking for oncology fellows and residents. The ENRICH program, designed for nurses who care for adolescent and young adult patients and survivors, was found to increase the FP knowledge score in two studies. The non-physician educational program significantly improved the FP-related knowledge and confidence of nurses and social workers.

Changes in Practice Behavior and Skills

The non-physician educational program demonstrated statistically significant improvements in the behavior of nurses and social workers in the 6 months after program completion, such as actively educating coworkers and providing resources

Table 2 Key data extracted from the five studies

Study (year)	Country	Program and target	Design and purpose	Sample and methods	Measures of program	Outcomes of program	Quality rating*
1. Huyghe et al. [32] (2009)	USA	BOF educational tool (oncology fellows and residents)	Small randomized trials: to evaluate the feasibility and efficacy of the computerized educational tool	19 oncology fellows and residents participated in this study. Half of the subjects used BOF before completing questionnaires, and half used it afterward	Participants filled out a professional version of the true/false knowledge test	Knowledge: Physicians who used BOF before filling out questionnaires scored significantly higher on the 20-item true/false knowledge test ($P = 0.006$)	2
2. Vadaparampil et al. [33] (2016)	USA	ENRICH program (nurses)	A quantitative nonrandomized study: to describe the impact of ENRICH for oncology nurses regarding AYA fertility and other reproductive health issues	77 participants completed a pre-test and post-test assessment and a 6-month follow-up survey assessing learner behaviors and institutional changes	Items were developed by an expert advisory panel	1. Knowledge: The mean pre-test and post-test total score increased from 58 to 77% correct ($P < 0.001$) 2. Learner perceptions and behavior: sharing strategies to initiate conversations with other providers (72%), reviewing current reproductive health practices (41%), forming a committee/taskforce to address reproductive health issues (20%), contacting national organizations for patient materials (37%), and financial resources (22%) 3. Institutional changes: created policies (30%), provided in-service education (37%), developed patient education materials (26%), initiated a fertility patient navigator role (28%), and collaborated with reproductive specialists (46%)	4
3. Takeuchi et al. [34] (2018)	Japan	Non-physician educational program (nurses, social workers)	A quantitative nonrandomized study: to evaluate the effects of the educational program for non-physician healthcare providers	Knowledge, confidence, institutional change, and self-practice of 124 participants were assessed pre-program, immediately post-program, and 6 months post-program	Confidence, knowledge, institutional change, and self-practice measures were self-designed for program evaluation	1. Confidence and knowledge: Scores for confidence and knowledge increased between pre-program and immediate post-program periods and between pre-program and 6-month post-program periods ($P < 0.01$) 2. Institutional change: held study groups with healthcare providers (15.8%),	4

Table 2 (continued)

Study (year)	Country	Program and target	Design and purpose	Sample and methods	Measures of program	Outcomes of program	Quality rating*
						held FP seminars for patients (6.6%), collaborated with reproductive specialists (36.8%), displayed brochures (22.4%), and announced fertility counseling (32.9%) 3. Self-practice: (1) Scores significantly increased (actively educate coworkers; disseminate information about fertility counseling; participate in educational programs; provide resources about FP) ($P < 0.01$), and (2) scores significantly decreased (asked patients about discussing fertility with their physicians) ($P < 0.05$)	
4. Quinn et al. [35] (2019)	USA	ENRICH program (nurses)	A quantitative nonrandomized study: to describe the impact of ENRICH on knowledge, perceived communication skills, and practice behaviors of oncology nurses	A 14-question pre-test and post-test was administered to assess changes in the knowledge of 233 nurses. Additionally, participants received a follow-up survey addressing communication skills and practice behaviors	Knowledge items were developed by content experts; program evaluation was created by CEU providers	1. Knowledge: Total score increased from 57 to 79% correct ($P < 0.0001$). 2. Program evaluation: 94% gained knowledge, and 95% felt the course increased their confidence in patient care; competencies were met: patient care, medical knowledge, practice-based learning and improvement, and interpersonal and communication skills 3. Communication skills and practice behaviors: Half of the participants often or always discussed risk of infertility with patients and discussed FP options. Two-thirds referred patients to reproductive specialists, and 72% documented those referrals; there was a significant increase in	4

Table 2 (continued)

Study (year)	Country	Program and target	Design and purpose	Sample and methods	Measures of program	Outcomes of program	Quality rating*
						communication skills in cohort 3 ($P < 0.001$)	
5. Winterling et al. [36] (2019)	Sweden	Fex-Talk (nurses)	A qualitative study: to evaluate the Fex-Talk intervention for nurses	The evaluation was based on participants' oral and written feedback regarding the content and organization of the intervention as well as on teachers' field notes from 5 educational events ($n = 140$)	The data were analyzed using a thematic approach	1. 4 themes were identified: increased awareness, need for knowledge, challenging discomfort, and dealing with external obstacles. 2. The intervention increased participants' awareness of patients' need to discuss fertility and of their own need for additional knowledge. 3. The role-play exercise was designed to overcome personal discomfort, and the Fex-Talk intervention was experienced positively by the participating nurses	5

*Quality score ranged from meeting none of five criteria (0) to meeting all criteria (5)

about FP ($P < 0.01$). However, the behavior of asking patients about discussing fertility with their physicians was significantly decreased ($P < 0.05$). There was a significant increase in communication skills following the ENRICH program ($P < 0.001$). Moreover, the Fex-Talk study reported that the 2-h educational program was experienced positively and increased the nurses' understanding of patients' needs.

Institutional Changes and Program Evaluation

The ENRICH program and the non-physician education program assessed the institutional changes after the completion of program, and the same changes were found including in-service education, developing patient education materials, and collaboration with reproductive specialists. Only the ENRICH program was evaluated, and 98% of nurses indicated they would recommend this course to others.

Discussion

To our knowledge, this is the first systematic review evaluating FP educational programs for healthcare providers who care for cancer patients. Though the educational programs for oncology healthcare providers are limited, the majority of programs were helpful for healthcare providers to acquire knowledge of FP and some programs were beneficial for promoting clinical practice. Among the five studies, three studies were quantitative nonrandomized studies, one study was a qualitative study, and only one study was a randomized controlled trial study; however, it had a very small sample size. More high-quality and homogeneous clinical trials about the educational programs are needed to conduct a meta-analysis to compare the effects of different educational programs and determine the most effective programs or interventions for oncology healthcare providers.

According to the ASCO guidelines, healthcare providers are recommended to provide timely oncofertility care for cancer patients. However, healthcare professionals' knowledge was found to be insufficient and education regarding FP is needed. In this review, only four training programs were included. It is surprising that even though the ASCO guidelines have been used for more than a decade, training programs for healthcare providers are still scarce. Three of the programs in this review were only relevant to nurses, one program was designed for social workers, and one was designed for oncology fellows and residents. It has been reported that oncologists lack the time to discuss fertility issues, and instead oncology

Table 3 Details of the four programs from the five studies

Studies	Programs	Learning theories or framework	Program duration	Program contents	Program forms
1. Huyghe et al.	BOF educational tool	No	No information	Damage from cancer therapies to sperm DNA and spermatogenesis; health of offspring; sperm banking procedures; assisted reproductive technology; ethical issues; communication skills using video; a checklist of topics to discuss with patients	1. Reading materials 2. Animation game 3. Video 4. Checklist
2. Vadaparampil et al. and Quinn et al.	ENRICH program	No	60–90 min over 8 weeks	An overview of topics and training website; risk of infertility due to cancer treatment; FP options for males and females; pediatric-specific considerations; alternative family-building options; sexual health; communication strategies; practical applications; ethical, legal, and psychosocial considerations	1. Web-based lecture 2. Textbook readings 3. Case studies 4. Learning assignments
3. Takeuchi et al.	Non-physician educational program	No	4 h	Infertility as a potential risk of cancer treatment; FP for males and females; psychosocial support	1. Lecture
4. Jeanette et al.	Fex-Talk	Kolb's experiential learning cycle	2 h	Sexuality and fertility	1. Lecture 2. Video 3. Role-play 4. Homework assignment

nurses and social workers were considered to be in an ideal position to discuss FP-related issues with cancer patients [22, 24]. Memorial Sloan Kettering Cancer Center (MSKCC) hired a clinical nurse specialist (CNS) to direct its Fertility Preservation and Parenthood after Cancer Treatment program in 2009, and an oncofertility nurse navigator (ONN) position was created in a hospital in Canada [25, 37]. Therefore, it is clear that oncology nurses are playing an increasingly important role in FP for cancer patients. However, some nurses and social workers believed that they should take the responsibility of providing follow-up care or support and physicians are supposed to initiate the discussion [24, 38]; thus, confusion about roles may be a barrier among healthcare providers in providing FP counseling and referrals. Clear guidelines or policies should be established in institutions, and specific roles for healthcare providers skilled in the area of oncofertility should be assigned.

Only the ENRICH program was a medium-term training programs that lasted 8 weeks; the other programs were short-term interventions that lasted several hours. Furthermore, three studies in this review conducted follow-up surveys after the completion of the program; however, the low response rate made analyzing the long-term effects of these educational programs difficult. Thus, long-term educational curricula with a proper arrangement (e.g., 60–90 min a week) and appropriate follow-ups should be developed to determine and improve the effectiveness and quality of training programs.

Several relative factors were found to hinder the discussion of FP for clinicians such as lack of knowledge, cultural and religious limitations, feeling uncomfortable, and lack of communication skills [39–41]. However, although all programs in this review provided FP-related knowledge for healthcare providers, communication strategies and psychosocial support were only taught in two programs, and FP-related ethical and legal issues were only mentioned in one program. It is clear that the current educational designs are not comprehensive enough to adequately train healthcare providers to provide oncofertility services. The oncofertility model of care (MOC) and its core components may offer a solution, as the MOC recommends all healthcare providers receive both oncofertility and communication skills trainings [42], and in the oncofertility training session, the necessity of psychological support was highlighted. Furthermore, healthcare professionals need to be trained to provide evidence-based and age-appropriate forms of FP information to cancer patients and their families in a way that makes both parties comfortable.

We suggest that future educational programs design a framework and develop a curriculum based on learning theories or good models such as the MOC.

When evaluating the program, learning outcomes were divided into four levels using Kirkpatrick's classical model: learner's satisfaction (level 1), changes in leaner's attitudes or perceptions (level 2A), learner's acquisition of knowledge or skills (level 2B), change in learner's behavior (level 3), change to clinical practice (level 4A), and benefits to patients (level 4B) [28]. It is clear that most of learning outcomes were mentioned in the five studies included in this review, but there was no standard measurement for the effectiveness of each educational program. Most of the authors used a self-made questionnaire to explore the knowledge level of healthcare providers and used a self-appraisal tool to rate their skills or attitude. It was difficult for us to make a horizontal comparison between these educational projects. Thus, a standard tool should be developed to measure the final educational effectiveness and level of learning outcome attained. Various evaluators, such as healthcare providers, cancer patients, and hospital managers, should be involved in the assessment process. A standard tool to measure FP knowledge or examine FP competency needs to be developed for healthcare providers.

There are some established oncology FP programs in the USA, such as the LIVESTRONG Fertility Program and the Fertility Preservation and Parenthood after Cancer Treatment program [43]. Although these programs cover FP training for healthcare providers, no data regarding their educational effectiveness was published. It is possible that these FP programs were multifaceted, and the specific impact of clinician education was difficult to determine from the evaluation of whole projects. Nevertheless, future FP projects that contain training interventions are suggested to provide some data about training effectiveness and offer insights on successful educational programs. Previously, the ENRICH program was the only training program that was evaluated for effectiveness [34]; however, a tailored ENRICH educational program for allied health professionals is being conducted by a team led by professor Quinn that will offer more training data to researchers in the near future [44].

Most of the educational programs in this review were conducted in America, a single program was conducted in Sweden, and the other in Japan. No educational projects have been reported in developing countries. More educational programs from different countries and cultural backgrounds are needed.

Study Limitations

Our review had some limitations. Firstly, we included a pilot randomized controlled trial study, three before-and-after studies, and one qualitative study in this review; however, we did not perform a meta-analysis with this data. Secondly, the effects reported may be subject to bias due to the weak reliability and validity of evaluation methods used in the studies included in this review.

Practice Implications

We believe that oncology healthcare providers, educators, and researchers will benefit from the following considerations. Firstly, educational programs should be designed according to learning theories or a theoretical framework to obtain a comprehensive training effect. Secondly, courses about FP should be increased in medical school education, and FP-related training needs to be added to continuing medical education to improve clinical FP practice. The most important part is that healthcare providers should be skilled at providing oncofertility care to cancer patients. Thirdly, standard tools should be developed and more high-quality randomized controlled trial studies on educational effectiveness should be conducted. Fourthly, more educational programs or interventions for healthcare professionals from different cultural backgrounds are needed. Fifthly, the roles and responsibilities of healthcare providers in oncofertility care should be clarified to eliminate role ambiguity and optimize the work of all healthcare workers. Finally, more established FP programs should display their educational data regarding healthcare providers and provide references and advice for other countries and regions.

Conclusions

In conclusion, the educational programs on FP effectively improved the knowledge of healthcare providers. However, the low number of programs and methodological limitations hindered the usefulness of comparisons between different programs. In order to increase the numbers of cancer patients of reproductive age taking part in FP, multidisciplinary healthcare professionals should be skilled in the area of reproductive health to provide sufficient support. More high-quality randomized controlled trial studies regarding FP training programs and the development, implementation, and evaluation of new programs based on different cultural backgrounds are needed.

Authors' Contributions Han-feng Zhang and Mika Miyashita contributed to the study conception and design. The literature search was performed by Han-feng Zhang, Qing-hua Jiang, and Jun Kako. The data analysis was performed by Han-feng Zhang, Gui-yu Huang, Kohei Kajiwara, and Jian-xia Lyu. Qing-hua Jiang and Gui-yu Huang contributed to the interpretation of the data. The first draft of the manuscript was written by Han-feng Zhang, and Mika Miyashita critically revised the draft. All authors commented on previous versions of the manuscript and read and approved the final manuscript.

Funding This study is supported by the Sichuan Science and Technology Program (2019YFH0105).

Data Availability The datasets generated and analyzed during the present study are available from the corresponding author on reasonable request.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no competing interests.

Research Involving Human Participants and/or Animals Not applicable

Informed Consent Not applicable

Consent for Publication Not applicable

References

1. Loren A, Mangu P, Beck L, Brennan L, Magdalinski AJ, Partridge AH, Quinn G, Wallace WH, Oktay K, American Society of Clinical Oncology (2013) Fertility preservation for patients with cancer: American Society of Clinical Oncology clinical practice guideline update. J Clin Oncol 31:2500–2510
2. Lee SJ, Schover LR, Partridge AH, Patrizio P, Wallace WH, Hagerty K, Beck LN, Brennan LV, Oktay K (2006) American Society of Clinical Oncology recommendations on fertility preservation in cancer patients. J Clin Oncol 24:2917–1931
3. Ajala T, Rafi J, Larsen-Disney P, Howell R (2010) Fertility preservation for cancer patients: a review. Obstet Gynecol Int 2010: 160386
4. Campo-Engelstein L (2010) Consistency in insurance coverage for iatrogenic conditions resulting from cancer treatment including fertility preservation. J Clin Oncol 28:1284–1286
5. Schover LR (2005) Sexuality and fertility after cancer. Hematology Am Soc Hematol Educ Progr 523–527
6. Johnson JA, Tough S, SOGC Genetics Committee (2012) Delayed child-bearing. J Obstet Gynaecol Can 34:80–93
7. Gorman JR, Bailey S, Pierce JP, Su HI (2012) How do you feel about fertility and parenthood? The voices of young female cancer survivors. J Cancer Surviv 6:200–209
8. Saito K, Suzuki K, Iwasaki A, Yumura Y, Kubota Y (2005) Sperm cryopreservation before cancer chemotherapy helps in the emotional battle against cancer. Cancer 104:521–524
9. Peate M, Meiser B, Cheah BC, Saunders C, Butow P, Thewes B, Hart R, Phillips KA, Hickey M, Friedlander M (2012) Making hard choices easier: a prospective, multicentre study to assess the efficacy of a fertility-related decision aid in young women with early-stage breast cancer. Br J Cancer 106:1053–1061
10. Rosen A, Rodriguez-Wallberg KA, Rosenzweig L (2009) Psychosocial distress in young cancer survivors. Semin Oncol Nurs 25:268–277
11. Peccatori FA, Azim HA Jr, Orecchia R et al (2013) Cancer, pregnancy and fertility: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. Ann Oncol 24(Suppl 6):vi160–vi170
12. Lambertini M, Del Mastro L, Pescio MC et al (2016) Cancer and fertility preservation: international recommendations from an expert meeting. BMC Med 14:1
13. Quinn GP, Vadaparampil ST, Lee JH, Jacobsen PB, Bepler G, Lancaster J, Keefe DL, Albrecht TL (2009) Physician referral for fertility preservation in oncology patients: a national study of practice behaviors. J Clin Oncol 27:5952–5957
14. Zhang H, Wang G, Cao M et al (2019) Level of knowledge and needs on fertility preservation in reproductive-aged male patients with cancer. J Cancer Educ
15. Flink DM, Sheeder J, Kondapalli LA (2017) A review of the oncology patient's challenges for utilizing fertility preservation services. J Adolesc Young Adult Oncol 6:31–44
16. Warner E, Yee S, Kennedy E, Glass K, Foong S, Seminsky M, Quan ML (2016) Oncofertility knowledge, attitudes, and practices of Canadian breast surgeons. Ann Surg Oncol 23:3850–3859
17. Panagiotopoulou N, Ghuman N, Sandher R, Herbert M, Stewart JA (2018) Barriers and facilitators towards fertility preservation care for cancer patients: a meta-synthesis. Eur J Cancer Care 27
18. Jones G, Hughes J, Mahmoodi N, Smith E, Skull J, Ledger W (2017) What factors hinder the decision-making process for women with cancer and contemplating fertility preservation treatment? Hum Reprod Update 23:433–457
19. Adams E, Hill E, Watson E (2013) Fertility preservation in cancer survivors: a national survey of oncologists' current knowledge, practice and attitudes. Br J Cancer 108:1602–1615
20. Arafa MA, Rabah DM (2011) Attitudes and practices of oncologists toward fertility preservation. J Pediatr Hematol Oncol 33:203–207
21. Takeuchi E, Kato M, Wada S, Yoshida S, Shimizu C, Miyoshi Y (2017) Physicians' practice of discussing fertility preservation with cancer patients and the associated attitudes and barriers. Support Care Cancer 25:1079–1085
22. Quinn GP, Vadaparampil ST, Gwede CK, Miree C, King LM, Clayton HB, Wilson C, Munster P (2007) Discussion of fertility preservation with newly diagnosed patients: oncologists' views. J Cancer Surviv 1:146–155
23. King L, Quinn GP, Vadaparampil ST, Gwede CK, Miree CA, Wilson C, Clayton H, Perrin K (2008) Oncology nurses' perceptions of barriers to discussion of fertility preservation with patients with cancer. Clin J Oncol Nurs 12:467–476
24. King L, Quinn GP, Vadaparampil ST, Miree CA, Wilson C, Clayton H, Zebrack B (2008) Oncology social workers' perceptions of barriers to discussing fertility preservation with cancer patients. Soc Work Health Care 47:479–501
25. Kelvin JF, Reinecke J (2012) Institutional approaches to implementing fertility preservation for cancer patients. Adv Exp Med Biol 732:165–173
26. Bradford NK, Walker R, Henney R, Inglis P, Chan RJ (2017) Improvements in clinical practice for fertility preservation among young cancer patients: results from bundled interventions. J Adolesc Young Adult Oncol 7:37–45
27. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JPA, Clarke M, Devereaux PJ, Kleijnen J, Moher D (2009) The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. J Clin Epidemiol 62:e1–e34
28. Kirkpatrick D, Kirkpatrick J (2006) Evaluating training programs: the four levels, 3rd edn. Berrett-Koehler Publishers Inc., San Francisco
29. Hong QN, Pluye P, Fàbregues S et al (2018) Mixed methods appraisal tool (MMAT) Canada: 2018
30. Pluye P, Gagnon M-P, Griffiths F, Johnson-Lafleur J (2009) A scoring system for appraising mixed methods research, and concomitantly appraising qualitative, quantitative and mixed methods primary studies in mixed studies reviews. Int J Nurs Studies 46: 529–547
31. Hong QN, Pluye P, Fàbregues S, Bartlett G, Boardman F, Cargo M, Dagenais P, Gagnon MP, Griffiths F, Nicolau B, O'Cathain A, Rousseau MC, Vedel I (2019) Improving the content validity of the mixed methods appraisal tool: a modified e-Delphi study. J Clin Epidemiol 111:49–59
32. Huyghe E, Martinetti P, Sui D, Schover LR (2009) Banking on fatherhood: pilot studies of a computerized educational tool on sperm banking before cancer treatment. Psychooncology 18: 1011–1014

33. Vadaparampil ST, Gwede CK, Meade C, Kelvin J, Reich RR, Reinecke J, Bowman M, Sehovic I, Quinn GP (2016) ENRICH: a promising oncology nurse training program to implement ASCO clinical practice guidelines on fertility for AYA cancer patients. Patient Educ Couns 99:1907–1910
34. Takeuchi E, Kato M, Miyata K, Suzuki N, Shimizu C, Okada H, Matsunaga N, Shimizu M, Moroi N, Fujisawa D, Mimura M, Miyoshi Y (2018) The effects of an educational program for non-physician health care providers regarding fertility preservation. Support Care Cancer 26:3447–3452
35. Quinn GP, Bowman Curci M, Reich RR, Gwede CK, Meade CD, ENRICH/ECHO Working Group, Vadaparampil ST (2019) Impact of a web-based reproductive health training program: ENRICH (Educating Nurses about Reproductive Issues in Cancer Healthcare). Psychooncology 28:1096–1101
36. Winterling J, Lampic C, Wettergren L (2019) Fex-Talk: a short educational intervention intended to enhance nurses' readiness to discuss fertility and sexuality with cancer patients. J Cancer Educ 1
37. Zwingerman R, Melenchuk K, McMahon E et al (2019) Expanding urgent oncofertility services for reproductive age women remote from a tertiary level fertility centre by use of telemedicine and an on-site nurse navigator. J Cancer Educ 2
38. Keim-Malpass J, Fitzhugh HS, Smith LP, Smith RP, Erickson J, Douvas MG, Thomas T, Petroni G, Duska L (2018) What is the role of the oncology nurse in fertility preservation counseling and education for young patients? J Cancer Educ 33:1301–1305
39. Rashedi AS, de Roo SF, Ataman LM et al (2018) Survey of fertility preservation options available to patients with cancer around the globe. J Glob Oncol 4:1–16
40. Zhang H, Wang G, Jiang B et al (2019) The knowledge, attitude, and self-reported behaviors of oncology physicians regarding fertility preservation in adult cancer patients. J Cancer Educ
41. Logan S, Perz J, Ussher J, Peate M, Anazodo A (2018) Clinician provision of oncofertility support in cancer patients of a reproductive age: a systematic review. Psycho-Oncology 27:748–756
42. Anazodo A, Laws P, Logan S, Saunders C, Travaglia J, Gerstl B, Bradford N, Cohn R, Birdsall M, Barr R, Suzuki N, Takae S, Marinho R, Xiao S, Qiong-Hua C, Mahajan N, Patil M, Gunasheela D, Smith K, Sender L, Melo C, Almeida-Santos T, Salama M, Appiah L, Su I, Lane S, Woodruff TK, Pacey A, Anderson RA, Shenfield F, Ledger W, Sullivan E (2019) How can we improve oncofertility care for patients? A systematic scoping review of current international practice and models of care. Hum Reprod Update 25:159–179
43. Reinecke JD, Kelvin JF, Arvey SR, Quinn GP, Levine J, Beck LN, Miller A (2012) Implementing a systematic approach to meeting patients' cancer and fertility needs: a review of the fertile hope centers of excellence program. J Oncol Pract 8:303–308
44. Quinn GP, Woodruff TK, Knapp CA, Bowman ML, Reinecke J, Vadaparampil ST (2016) Expanding the oncofertility workforce: training allied health professionals to improve health outcomes for adolescents and young adults. J Adolesc Young Adult Oncol 5: 292–296

恶性肿瘤患者生育力保护服务研究进展

张含凤[1]，黄桂玉[2]，方迎红[1]，阮礼凤[1]，白洪芳[1]，张健[2]，江庆华[2]

Research progress of fertility preservation service for patients with malignant tumor *Zhang Hanfeng, Huang Guiyu, Fang Yinghong, Ruan Lifeng, Bai Hongfang, Zhang Jian, Jiang Qinghua*

摘要：从肿瘤治疗对生育力的影响、肿瘤患者生育力保护相关指南、国外肿瘤患者生育力保护服务研究热点和进展等进行综述，旨在基于国外研究成果、局限性及国内现况，为开展肿瘤患者生育力保护相关研究服务及出台肿瘤患者生育力保护共识或指南提供参考。

关键词：恶性肿瘤； 生育； 生育力保护； 综述文献

中图分类号：R473.73 **文献标识码**：A **DOI**：10.3870/j.issn.1001-4152.2020.09.103

生育力保护又称生育力保存，是指对受手术创伤、放化疗、遗传、年龄等因素影响预期或已经出现生殖腺功能减退或丧失患者，通过手术、药物或冷冻技术干预其精子、卵子或生殖腺体，保护其生殖内分泌功能，并最终生育遗传学后代的一种助孕技术[1]。随着肿瘤治疗的发展，肿瘤患者生存率提高，生育力作为衡量肿瘤患者远期生活质量的一个重要方面日益受到重视[2]。接受肿瘤治疗后，男性患者可出现暂时性或永久性无精子症，而女性患者可能无法产生成熟的卵子或出现卵巢早衰，这都极大地影响患者的生育力[3]。据文献报道，保留生育力的肿瘤患者能更积极地对抗癌症，而丧失生育力的患者则会经历巨大的痛苦、悲伤等负性情绪，患者有保留生育能力的强烈愿望[4]。为了有效保护肿瘤患者的生育力，Woodruff[5]在 2007 年首次提出“肿瘤生育(Oncofertility)”整合医学理念，即通过肿瘤学专家、生殖内分泌学家、遗传学家和心理学家等多学科团队成员为肿瘤患者提供最权威、及时的生育力保护方案并实施。在我国，由于受传宗接代文化影响，患者若失去生育力会承受来自家庭、社会的多重压力。加之国内二胎政策开放，越来越多的患者希望可以再次生育，使得育龄肿瘤患者的生育力保护有更重要的现实意义[6]。然而，目前国内医务人员对肿瘤患者的关注主要集中在治疗效果和生存率上，对患者生育力风险及保护的重视程度整体偏低，亦缺少肿瘤患者生育力保护服务的相关临床文献。鉴此，笔者对国外肿瘤患者生育力保护服务的文献进行综述，为我国开展肿瘤患者生育力服务及建立生育力保护相关共识或指南提供参考。

1 肿瘤治疗对生育力的影响

生育力损害是治疗恶性肿瘤引起的严重毒副反应，研究表明，40%～80%的女性肿瘤患者和 30%～75%的男性肿瘤患者会面临不孕的风险[7]。肿瘤治疗后患者生育力下降和永久性不孕发生率因多种因素而异，其中化疗和放疗对生育力的影响程度取决于化疗药物或放疗靶区大小/位置、总剂量、单次剂量强度、给药方法(口服和静脉注射)、疾病类型、年龄、性别等。对男性肿瘤患者，疾病本身(如睾丸癌和霍奇金淋巴瘤)、治疗引起的解剖学问题(如逆行射精或无射精)和生殖干细胞受损都会损害生育力。男性患者在化疗或放疗后可见精子数量、活力、形态变化和 DNA 完整性受损。对女性肿瘤患者，任何减少原始卵泡数量、影响激素平衡或干扰卵巢、输卵管、子宫或子宫颈功能的肿瘤治疗都可能损害生育能力，其中手术或放疗引起的子宫、子宫颈、阴道解剖或血管变化会降低自然受孕的概率，因此需要辅助生殖技术[8]。免疫靶向治疗、激素治疗等治疗方式也会影响患者的生育能力，但仍需更多的临床证据。

2 肿瘤患者生育力保护技术与生育风险

2.1 肿瘤患者生育力保护技术 对青春期后期和成年男性肿瘤患者，精子冷冻保存是一种常规、可靠和成熟的生育力保护方法。由于肿瘤治疗后精子质量和精子 DNA 完整性受到影响，因此美国临床肿瘤学学会(American Society of Clinical Oncology，ASCO)指南强烈建议患者在治疗前尽快完成精子冷冻。而其他生育力保护方法，如睾丸组织冷冻保存、再植或移植，仅作为临床试验或批准的实验方案的一部分进行[9]。

对成年女性肿瘤患者，ASCO 指南推荐胚胎或卵母细胞冷冻保存作为生育保存的标准策略[9]。其中，胚胎冷冻适合已有配偶的患者，卵母细胞冷冻适合不希望使用捐赠精子的单身女性患者或对胚胎冷冻有宗教或伦理排斥的患者。对盆腔放疗女性患者也可采用卵巢移位技术进行生育力保护，但是由于放疗散射仍可能影响卵巢功能，所以这项技术的妊娠成功率难以保障。其次，卵巢组织冷冻作为处于实验阶段的保存生育能力的方法，具有不刺激卵巢、可随时进行、

作者单位：四川省肿瘤医院研究所/四川省癌症防治中心/电子科技大学医学院/放射肿瘤学四川省重点实验室 1.腹盆放疗病区 2.护理部(四川 成都，610041)

张含凤：女，博士在读，主管护师，护士长

通信作者：江庆华，569458942@qq.com

科研项目：四川省科技厅国际科技创新合作项目(2019YFH0105)

收稿：2019－ －；修回：2020－01－28

不受有无配偶限制的优势，是未来非常有前景的一项生育力保护技术。另外，指南指出卵巢抑制方法不能替代已经被证实有效的胚胎或卵母细胞冷冻保存技术为患者进行生育力保存[9-10]。

对儿童肿瘤患者，若为青春期后儿童，则推荐精子或卵母细胞冷冻保存；而对青春期前儿童，卵巢或睾丸组织冷冻保存是唯一的生育力保存选择，但这两项技术目前均处于实验阶段[11]。

2.2 肿瘤患者生育力保护后生育风险 由于采用生育力保护技术后患者或其配偶受孕受多方面的影响，目前没有关于患者进行生育力保护之后受孕和风险概率的明确数据。指南指出，大多数生育保存方法和患者怀孕并未导致疾病复发风险增加，包括对激素敏感的肿瘤患者。同时，除遗传性遗传综合征（Hereditary Genetic Syndromes）等特殊疾病外，没有证据表明肿瘤史、肿瘤治疗或生育力保护干预会增加子代癌症或先天性异常的风险[12]。因此，建议肿瘤医生联合生殖专家全面告知患者有关肿瘤治疗、生育保存可选方案以及辅助生殖技术对后代可能产生的影响，让患者在充分掌握这些信息的基础上根据自身条件及生育愿望作出生育力保护决策。

3 肿瘤患者生育力保护指南

3.1 国际肿瘤患者生育力保护指南 由于生育力风险是肿瘤治疗中需要涉及的问题之一，国际组织纷纷制定生育力保护指南以规范临床实践。2005 年，美国生殖医学协会（American Society of Reproductive Medicine，ASRM）发表论文强调，肿瘤医生应在治疗前告知患者生育力保存和未来生殖的选择，并建议为避免有遗传性癌症高风险后代的出生，可以实施胚胎植入前的遗传诊断[13]。2006 年，ASCO 正式发布第一个肿瘤患者生育力保护指南[8]。随后，各大专业协会，如美国儿科协会和欧洲肿瘤医学协会等相继发布指南。2007 年，国际生育力保护协会（International Society for Fertility Preservation，ISFP）成立，并于 2012 年出台淋巴瘤、白血病和乳腺癌患者生育力保护指南。虽然这些指南在内容上有细微差别，但他们都具有相同的核心原则，即将肿瘤患者生育力保护纳入临床实践。指南要求，卫生保健提供者在患者治疗前应尽早告知，并与育龄肿瘤患者或儿童患者的父母/监护人就生育风险和可选择的生育保护策略展开讨论，及时将有生育愿望的患者转介给生殖专家。

3.2 亚洲国家生育力保护指南概况 2012 年，日本率先成立生育力保护协会（Japan Society for Fertility Preservation，JSFP）。之后，韩国和印度分别于 2013 年和 2014 年成立生育力保护协会。2015 年，亚洲生育力保护协会正式成立，协会包括亚洲 14 个国家，并于 2016 年在越南召开第一届亚洲生育力保护年会。我国在 2017 年成立中国妇幼保健生育力保存专业委员会。

随着生育力保护协会的相继成立，亚洲各国的生育力保护指南相继出台。日本生殖医学学会（Japan Society of Reproductive Medicine，JSRM）和日本妇产科学会（Japan Society of Obstetrics and Gynecology，JSOG）分别在 2013 年和 2014 年出台女性患者生育力保护指南。2017 年，日本临床肿瘤学会（Japan Society of Clinical Oncology，JSCO）出台针对儿童、青少年和青年生育力保护的指南。同年，韩国生育力保护协会发布韩国生育力保护临床指南，并随后制定乳腺癌、血液肿瘤及妇科恶性肿瘤患者的生育力保护指南。目前印度和中国虽然有专业的生育力保护协会，但尚未出台生育力保护相关指南或共识。

3.3 指南中卫生保健提供者的角色和职责 在 2006 年 ASCO 出版的肿瘤患者生育力保护指南中，肿瘤医生作为唯一的主体被建议进行肿瘤患者生育力保护的告知、讨论和转介等服务。但在 2013 年 ASCO 更新的指南中，则将讨论、转介育龄肿瘤患者的责任扩展到所有卫生保健提供者，包括护理人员[2]。卫生保健提供者需要履行的角色和职责涵盖四个方面。第一，应做好告知、与患者开展生育风险讨论的各项准备。一旦患者被诊断为恶性肿瘤，讨论需尽快进行。第二，鼓励患者参与现有的临床研究和登记，以进一步明确开展的干预措施和策略的安全性、有效性。第三，将有生育愿望或对生育保护犹豫的患者尽快转介给生殖专家。第四，当患者对潜在的生育风险存在负性情绪时，医护人员应将其转介给心理学或社会学专家进行干预[9]。

自肿瘤患者生育力保护指南颁布以来，肿瘤医生常被作为为患者提供生育力保护服务的主体，但由于护理人员是与患者接触最多的人员，逐渐被认为是与患者沟通生育力保护的最适宜人选[14]。2009 年，美国纪念斯隆-凯特琳癌症中心安排临床专科护士专职负责患者生育力保护项目，包括为患者提供生育力保护教育、咨询、转诊服务，并协调肿瘤科团队成员和生殖专家的工作进度[15]。之后，针对护理人员的生育力保护专项培训项目也陆续开展[16]。护理人员在肿瘤生育领域发挥着越来越重要的作用，但具体角色职责和范畴尚未有明确的界定，还需要依据不同国家政策和文化背景进行设置。

4 肿瘤患者生育力保护服务的研究趋势

4.1 各国横断面调查切入点及现状 从近 10 年的文献可以看出，日本、美国、英国、加拿大、瑞典和法国 6 个国家进行了 12 项关于肿瘤患者生育力保护的全国性横断面调查。其中，8 项研究的调查对象为医疗从业人员，包括肿瘤科医生、儿科内分泌专家和血液肿瘤专家；其他 4 项研究的调查对象是癌症患者和生育机构。对医疗从业者，侧重于描述医生对肿瘤患者生育力保护的知识、态度、经验、感受和行为现状；了解医生将患者转介给生殖专家的现况以及探讨医生向育龄患者告知和讨论生育力保存问题的影响因素。

另外有2项研究从癌症患者的角度入手，调查患者生育力保存的意愿及影响因素。还有2项对生育机构的研究则调查了加拿大生育诊所为肿瘤患者提供的生育保护服务现状，包括生育力保护服务的可获得性、可负担性和利用率。纵观这些全国性调查结果，除瑞典肿瘤医生和血液肿瘤专家定期与肿瘤患者讨论生育风险外，其他研究结果均提示目前为肿瘤患者提供的生育力保护服务不足，其中最为凸显的是医疗从业人员对生育力保护知识储存不足，未依照指南对患者进行生育风险告知及转介给生殖专家。需要指出的是，12项全国性横断面调查中有6项研究聚焦于女性肿瘤患者，2项研究关注青少年和青年肿瘤患者，而无以男性肿瘤患者为主要研究对象开展的普查。

在我国，以医护人员或肿瘤患者为对象的临床研究很少，文献多集中于生殖专家对生育力保护技术的探讨，尚无全国性横断面普查，仅有的一项关于人类精子库的调查揭示了男性肿瘤患者生育力保存数量非常低的现况[17]。上海、江苏人类精子库在6～7年分别只有12例和17例肿瘤患者冷冻精液，湖南人类精子库11年仅97例肿瘤患者进行精液冻存。相较于男性肿瘤患者的生育力保存，女性肿瘤患者生育力保存技术更为复杂和耗时，因此保存比例更低。由此可见，我国肿瘤患者生育力保存的数量与大量育龄肿瘤患者的基数并不匹配。

4.2 肿瘤患者生育力保护服务研究的热点

4.2.1 生育力保护的告知和讨论 据文献显示，在沙特阿拉伯、日本和英国，与肿瘤患者讨论生育问题的肿瘤医生比例分别为42％、42.7％和97％[18-20]。由此可见，虽然多项国际指南已出台十余年，但目前肿瘤患者的生育力保护实践仍不乐观。为促进医护人员更好地完成生育力保护的告知和讨论工作，学者围绕告知和讨论的时机、沟通形式等展开研究。在讨论时机方面，一致认为肿瘤医生应在患者诊断后不久提供明确和客观的生育力保护信息，并将患者转介给生殖专家[21]。虽然40％的临床医生认为患者应首先提出生育力保存的话题[22]，但也有不少肿瘤专科护士表示应该由肿瘤医生负责发起生育力保存的相关讨论[23]。在沟通形式方面，有研究显示，97％的医生只使用语言交流[24]，而患者则希望从医护人员、书面材料及互联网多种途径获取生育力保护信息[25]。

4.2.2 肿瘤患者的转介服务 肿瘤医生及时将育龄肿瘤患者转介给生殖专家是肿瘤患者生育力保存中至关重要的一环。然而，研究表明，仅46.7％的肿瘤医生总是或经常转介患者给生殖专家[26]。由此可见，肿瘤患者转介到生殖专家的实际情况与指南要求有很大差距。为此，学者也积极寻找影响患者转介的相关因素。首先是机构因素，没有转诊流程和转诊途径，或者机构无患者生育力保护的相关理念等因素会影响转介[27]。其次是人为因素，具有丰富生育力保护知识的肿瘤医生和获取足够生育力保护信息的患者更倾向于转介；当肿瘤医生与生殖专家结成联盟时，患者的转介率会增加[28]。

4.2.3 患者支持系统 研究证实，无论是男性还是女性肿瘤患者，暂时性或永久性不孕的风险都会为其带来抑郁、焦虑等负性心理，而当他们缺乏生育信息和支持时更容易产生负面情绪。因此，患者希望获得信息、服务、心理社会等多方面的支持，包括获取生育风险、生育力保护的益处、不良反应和成功率等信息，并与能够提供情感和决策支持的同龄人、配偶和家人一同讨论生育问题[29]。同时，研究发现，为患者提供决策辅助能显著增加其生育保护知识，减少决策冲突，进而提高生育力保护率，并在治疗后12个月表现出更低的后悔情绪[30]。但目前文献中提及的9种患者决策辅助工具只有2种针对肿瘤患者，且处于开发状态，实际应用效果还需要进一步确认[31]。

4.2.4 生育力保护知识培训 国外研究发现，大多数肿瘤医生缺乏生育力保护知识，且他们很少或从未接受过生育力保护相关培训，不具备足够的能力与患者进行生育力保护事宜的讨论[17,32]。对非肿瘤专科医生的调查发现，妇科医生具有良好的生育力保护知识并积极转介患者[33]，但血液学医生表示缺乏生育力保护的相关培训[34]。对医疗从业人员的调查显示，21％接受过生育力保护培训，但其中医生和护士比例仅为37％和31％[35]。由此可见，与肿瘤患者日常接触的国外医务人员在生育力保护知识层面均存在不同程度的匮乏，但目前关于生育力保护知识培训或教育类干预项目的文献很少。我国调查显示，肿瘤专科医生的生育力保护知识偏低，且80％以上的医生表示未参加过生育力保护相关培训[36]。

4.2.5 生育力保护服务的影响因素 整体而言，目前为肿瘤患者提供的生育支持服务尚未达到指南的标准，许多临床医生没有向符合条件的患者提供生育力保护服务，患者也缺乏肿瘤生育支持[37]。究其原因，从机构层面，第一，机构缺乏生育力保护政策或指导意见。美国30个机构中只有4个机构(13.3％)有政策要求医护人员为患者提供生育力保护服务[38]。75％的临床医生表示所在机构缺乏生育力保护相关指导意见[39]。第二，生育力保护费用未被保险或机构覆盖。ASCO在2017年调查28个国家的40家机构，仅11个机构表示患者的生育力保护费用由保险或国家保健系统支付，但超过70％的机构需要患者自行支付费用[40]。

从医护人员层面，生育力知识和信息不足是提供生育力保护服务最大的阻碍因素[32]。其次，有的医生因为文化因素对讨论生育问题很抵触或有明显的不舒适感，特别是对儿童和青少年患者[40]。再者，有的医生因生育力保护会延迟肿瘤治疗或因患者疾病

分期晚或因患者已经有子女等原因未向患者告知生育风险和生育力保护相关信息。另外，生育力保护涉及伦理问题以及患者缺乏足够的信息来作出明智的生育决策等也是影响因素[41-42]。

5　展望

5.1　亟待出台生育力保护专家共识或者指南　考虑到我国特殊的文化背景和医患关系，迫切需要在借鉴已颁布的国际指南基础上，因地制宜地制定我国肿瘤患者生育力保护专家共识或指南，在行业内建立规范，保证医护人员为患者进行充分的生育风险和保护策略告知，提供及时的生育力保护服务，避免因告知不全带来潜在的纠纷隐患。同时专家共识或指南应有可操作性，明确多学科团队成员构成，清晰界定不同成员的工作角色、工作范畴和具体职责，细化生育力保护服务各个环节的具体要求，建立安全可靠的转介途径。另外，由于费用是影响患者进行生育力保护的首要阻碍因素[38]，因此有必要从国家层面考虑是否将此费用纳入医疗保险报销条目或增设其他资助扶持项目以减轻患者经济负担。

5.2　在校教育联合继续教育，拓宽专业能力宽度和深度　建议我国医学院在课程设置上拓宽生育力保护知识的宽度和深度，除常规讲授肿瘤治疗对生育力的损害机制外，还需纳入生育力保护时机、适应证、保护方法及策略等知识，加大对医学生生育力保护意识的培养力度，让学生充分认识到肿瘤患者生育力的潜在风险和进行生育力保护的重要意义。强化在岗肿瘤专科医护人员的继续教育培训，可通过肿瘤专科会议、专题培训或院内教育等多种形式进行生育力保护专项培训，转变医护人员的传统观念，正确认识肿瘤患者生育力保护的重要性和必要性，联合生殖专家、心理专家为患者提供详细的生育力保护信息及需要的心理支持，进而协助患者作出理性的生育力保护决策。医护人员为肿瘤患者提供生育力保存服务需要的能力框架已经制定[43]，对医护人员的培训内容可借鉴这个框架进行设置。除专科能力培养外，还建议设置提升沟通技能的课程。希望通过在校教育和继续教育，让肿瘤专科医护人员增加生殖专科知识，提升风险意识，为患者提供个性化、适龄化、高质量的生育力保护服务。

5.3　开发决策辅助工具　目前国内外尚未有成熟的决策辅助工具，因此有必要开发适合我国国情并有助于肿瘤患者理解和权衡生育力保护选项的决策辅助工具，或开展协助患者进行决策的干预项目，为患者提供足够的决策支撑；同时也能缓解医生告知和讨论生育力保护问题的压力。

综上所述，肿瘤患者生育力保护的告知和转介不足是目前国际上存在的共性问题，而目前国内对肿瘤患者生育力保护的关注甚少。有必要借鉴国外经验并结合国情和病种特点，制定肿瘤患者生育力保护相关政策或指南，明确医护人员在生育力保护中的角色和职责，加强医护人员生育力保护培训，从而为不同肿瘤患者或家属提供专业的生育力保护服务，保障患者决策知情同意和自主选择权，提高远期生活质量。

参考文献：

[1]　黄国宁. 生育力保护概述[J]. 实用妇产科杂志，2016，32(4)：241-242.

[2]　Loren A W，Mangu P B，Beck L N，et al. Fertility preservation for patients with cancer：American Society of Clinical Oncology clinical practice guideline update[J]. J Clin Oncol，2013，31(19)：2500-2510.

[3]　Ajala T，Rafi J，Larsen-Disney P，et al. Fertility preservation for cancer patients：a review[J]. Obstet Gynecol Int，2010(2)：160386.

[4]　Rosen A，Rodriguez-Wallberg K A，Rosenzweig L. Psychosocial distress in young cancer survivors[J]. Semin Oncol Nurs，2009，25(4)：268-277.

[5]　Woodruff T K. The emergence of a new interdiscipline：oncofertility[M]//Woodruff T K，Snyder K A. Oncofertility. Boston，MA：Springer，2007：3-11.

[6]　刘秀儒，林霞. 女性癌症患者生育忧虑研究进展[J]. 护理学杂志，2017，32(16)：100-103.

[7]　Dyer K E，Quinn G P. Cancer and fertility preservation in Puerto Rico：a qualitative study of healthcare provider perceptions[J]. Support Care Cancer，2016，24(8)：3353-3360.

[8]　Lee S J，Schover L R，Partridge A H，et al. American Society of Clinical Oncology recommendations on fertility preservation in cancer patients[J]. J Clin Oncol，2006，24(18)：2917-1931.

[9]　Oktay K，Harvey B E，Partridge A H，et al. Fertility preservation in patients with cancer：ASCO clinical practice guideline update[J]. J Clin Oncol，2018，36(19)：1994-2001.

[10]　徐珂. 恶性肿瘤患者的生育保护[J]. 肿瘤预防与治疗，2018，31(3)：219-226.

[11]　刘照南，徐迎春，张凤春. 2018 美国临床肿瘤学会关于恶性肿瘤患者生育能力保护的临床实践指南解读[J]. 临床肿瘤学杂志，2019，24(5)：468-473.

[12]　Fosså S D，Magelssen H，Melve K，et al. Parenthood in survivors after adulthood cancer and perinatal health in their offspring：a preliminary report[J]. J Natl Cancer Inst Monogr，2005(34)：77-82.

[13]　Ethics Committee of the American Society for Reproductive Medicine. Fertility preservation and reproduction in cancer patients[J]. Fertil Steril，2005，83(6)：1622-1628.

[14]　Quinn G P，Vadaparampil S T，Gwede C K，et al. Discussion of fertility preservation with newly diagnosed patients：oncologists' views[J]. J Cancer Surviv，2007，1(2)：146-155.

[15]　Kelvin J F，Reinecke J. Institutional approaches to implementing fertility preservation for cancer patients[J]. Adv Exp Med Biol，2012，732：165-173.

[16] Vadaparampil S T, Gwede C K, Meade C, et al. ENRICH: a promising oncology nurse training program to implement ASCO clinical practice guidelines on fertility for AYA cancer patients[J]. Patient Educ Couns,2016,99(11):1907-1910.
[17] 傅龙龙,张开舒.男性青少年肿瘤患者的生育力保护[J].中华男科学杂志,2017,23(3):262-266.
[18] Adams E, Hill E, Watson E. Fertility preservation in cancer survivors: a national survey of oncologists' current knowledge, practice and attitudes[J]. Br J Cancer, 2013,108(8):1602-1615.
[19] Arafa M A, Rabah D M. Attitudes and practices of oncologists toward fertility preservation[J]. J Pediatr Hematol Oncol,2011,33(3):203-207.
[20] Takeuchi E, Kato M, Wada S, et al. Physicians' practice of discussing fertility preservation with cancer patients and the associated attitudes and barriers[J]. Support Care Cancer,2017,25(4):1079-1085.
[21] Garvelink M M, Ter Kuile M M, Louwé L A, et al. A Delphi consensus study among patients and clinicians in the Netherlands on the procedure of informing young breast cancer patients about Fertility Preservation[J]. Acta Oncol,2012,51(8):1062-1069.
[22] Ghorbani B, Madahi P, Shirazi E, et al. Iranian oncologists' attitude towards fertility preservation in a sample group[J]. J Reprod Infertil,2011,12(1):33-36.
[23] Murray A N, Chrisler J C, Robbins M L. Oncology nurses report attitudes and barriers to discussing fertility preservation[J]. Clin J Oncol Nurs,2016,20(4):E93-E99.
[24] Yee S, Fuller-Thomson E, Lau A, et al. Fertility preservation practices among Ontario oncologists[J]. J Cancer Educ,2012,27(2):362-368.
[25] 张含凤,王国蓉,曹茂秋,等.育龄男性癌症患者生育力保护知识及需求调查[J].护理学杂志,2019,34(3):23-27.
[26] Quinn G P, Vadaparampil S T, Lee J H, et al. Physician referral for fertility preservation in oncology patients: a national study of practice behaviors[J]. J Clin Oncol,2009,27(35):5952-5957.
[27] Preaubert L, Pibarot M, Courbiere B. Can we improve referrals for fertility preservation? Evolution of practices after the creation of a fertility network[J]. Future Oncol,2016,12(19):2175-2177.
[28] Louwé L, Stiggelbout A, Overbeek A, et al. Factors associated with frequency of discussion of or referral for counselling about fertility issues in female cancer patients[J]. Eur J Cancer Care,2018,27(1):e12602.
[29] Logan S, Perz J, Ussher J M, et al. A systematic review of patient oncofertility support needs in reproductive cancer patients aged 14 to 45 years of age[J]. Psychooncology,2018,27(2):401-409.
[30] Peate M, Meiser B, Cheah B C, et al. Making hard choices easier: a prospective, multicentre study to assess the efficacy of a fertility-related decision aid in young women with early-stage breast cancer[J]. Br J Cancer,2012,106(6):1053-1061.
[31] Wang Y, Anazodo A, Logan S. Systematic review of fertility preservation patient decision aids for cancer patients[J]. Psychooncology,2019,28(3):459-467.
[32] Chung J P, Lao T T, Li T C. Evaluation of the awareness of, attitude to, and knowledge about fertility preservation in cancer patients among clinical practitioners in Hong Kong[J]. Hong Kong Med J,2017,23(6):556-561.
[33] Duncan F E, Jozefik J K, Kim A M, et al. The gynecologist has a unique role in providing oncofertility care to young cancer patients[J]. US Obstet Gynaecol,2011,6(1):24-34.
[34] Gilbert E, Adams A, Mehanna H, et al. Who should be offered sperm banking for fertility preservation? A survey of UK oncologists and haematologists[J]. Ann Oncol,2011,22(5):1209-1214.
[35] Ussher J M, Cummings J, Dryden A, et al. Talking about fertility in the context of cancer: health care professional perspectives[J]. Eur J Cancer Care (Engl),2016,25(1):99-111.
[36] Zhang H, Wang G, Jiang B, et al. The knowledge, attitude, and self-reported behaviors of oncology physicians regarding fertility preservation in adult cancer patients[J]. J Cancer Educ, 2019, doi: 10. 1007/s13187-019-01567-6.
[37] Logan S, Perz J, Ussher J, et al. Clinician provision of oncofertility support in cancer patients of a reproductive age: a systematic review[J]. Psychooncology,2018,27(3):748-756.
[38] Clayman M L, Harper M M, Quinn G P, et al. Oncofertility resources at NCI-designated comprehensive cancer centers[J]. J Natl Compr Canc Netw,2013,11(12):1504-1509.
[39] Vadaparampil S T, Quinn G P, Clayton H B, et al. Institutional availability of fertility preservation[J]. Clin Pediatr (Phila),2008,47(3):302-305.
[40] Rashedi A S, de Roo S F, Ataman L M, et al. Survey of fertility preservation options available to patients with cancer around the globe[J]. J Glob Oncol,2018,4:1-16.
[41] Flink D M, Sheeder J, Kondapalli L A. A review of the oncology patient's challenges for utilizing fertility preservation services[J]. J Adolesc Young Adult Oncol,2017,6(1):31-44.
[42] 郑丹萍,董鑫,王晓晶.年轻乳腺癌患者生育计划及知识与治疗决策的研究[J].护理学杂志,2015,30(22):31-34.
[43] Anazodo A, Laws P, Logan S, et al. The development of an international oncofertility competency framework: a model to increase oncofertility implementation. oncologist[J]. Oncologist,2019,24(12):e1450-e1459.

（本文编辑　宋春燕）

Observational Study

Medicine®

OPEN

Importance and safety of autologous sperm cryopreservation for fertility preservation in young male patients with cancer

Yinfeng Li, MSc[a], Jian Zhang, BS[a], Hanfeng Zhang, PHD[a], Bo Liu, MS[b], Guorong Wang, PHD[a], Maoqiu Cao, BS[a], Bencui Fu, BS[a], Hui Li, BS[b], Qinghua Jiang, BS[a], Lin Yu, BS[b], Yang Xian, BS[b], Bizhen Su, BS[b], Xiaohui Jiang, PHD[b,*]

Abstract

With development of tumor treatment, survival time of patients with cancer is significantly prolonged. Therefore, the current emphasis is not only the survival, but also the quality of life, especially, it is crucial for young male cancer patients who are unmarried and maintaining fertility. However, the awareness of fertility preservation for these patients is currently insufficient.

To give physician and cancer patients more clear understanding of the importance and safety of sperm cryopreservation, so that achieve patient fertility benefits.

First, the knowledge level and attitudes about fertility preservation were investigated by surveying 332 cancer patients and 103 medical staff with questionnaires. Second, 30 male cancer patients (experimental group) and 30 normal donors (control group) were selected and their sperm samples were cryopreserved. The sperm quality was compared between cancer patients and normal donors, before and after antitumor treatment in the cancer patients, and before and after sperm cryopreservation in both groups.

In the questionnaire survey, we found that there were 70% to 80% of medical staffs and cancer patients lacked knowledge of fertility preservation, and 27.7% of patients worried that tumor and sperm cryopreservation might affect their offspring. In the sperm preservative experiment, we found that sperm quality in cancer patients was further damaged after radiotherapy/chemotherapy in addition to tumor itself had a negative effect. However, sperm deoxyribonucleic acid fragments were not affected by sperm cryopreservation although there were significant differences in sperm quality before and after sperm preservation in both groups.

Radiotherapy/chemotherapy would further damage sperm quality of young male cancer patients. Medical staff should be aware of importance of sperm cryopreservation for fertility preservation for these patients. It is also necessary that medical staff should inform the patient about the safety of sperm freezing and guide the patient to participate in sperm cryopreservation.

Abbreviations: FP = fertility preservation, PR = progressive sperm motility, SDF = sperm DNA fragmentation.

Keywords: cancer, deoxyribonucleic acid, fertility preservation, sperm cryopreservation

Editor: Weimin Guo.

YL and JZ contributed equally to this work and should be the co-first authors.

Jian Zhang is currently receiving a grant (130225) from the Scientific Research of Sichuan Province Health Department, for the remaining authors none were declared.

The authors have no conflicts of interest to disclose.

[a] Sichuan Cancer Hospital & Institute, Sichuan Cancer Center, School of Medicine, University of Electronic Science and Technology of China,
[b] Department of Human Sperm Bank, West China Second University Hospital of Sichuan University, Chengdu, Sichuan, China; Key Laboratory of Birth Defects and Related Diseases of Women and Children (Sichuan University), Ministry of Education, Chengdu, China.

[*] Correspondence: Xiaohui Jiang, West China Second University Hospital of Sichuan Hospital, Chengdu, Sichuan, China (e-mail: 3289603921@qq.com).

How to cite this article: Yinfeng L, Zhang J, Zhang H, Liu B, Wang G, Cao M, Fu B, Li H, Jiang Q, Lin Y, Xian Y, Su B, Jiang X. Importance and safety of autologous sperm cryopreservation for fertility preservation in young male patients with cancer. Medicine 2020;99:15(e19589).

Received: 6 May 2019 / Received in final form: 3 February 2020 / Accepted: 18 February 2020

http://dx.doi.org/10.1097/MD.0000000000019589

Key Points

What is already known about the topic?

- Globally, cancer has become second leading cause of death, the number of cancer-related death was reported to be 8.8 million in 2015. But the survival time of patients with cancer is significantly prolonged. The current emphasis is not only the survival, but also the quality of life, especially it is crucial for men who are unmarried, maintaining fertility. The damage to male fertility is not only by tumor itself, but also by the chemo-radiotherapy/targeted therapy, people's awareness of fertility preservation is insufficient. The main reason may be contributed to that both medical staffs and patients have no enough knowledge and correct attitude about fertility preservation.

What this paper adds

- The present study showed that sperm concentration and/or progressive sperm motility in tumor patients were significantly lower while sperm DNA fragments were significantly more in cancer patients than those in normal donors.

- Cryopreservation can reduce sperm motility, but did not influence the potential fertility by analyzing the semen parameters.
- There was no significant difference in DNA fragment index before and after freezing, suggesting that the freezing technique is safe and reliable and does not affect the patient's genetic function.

1. Introduction

Globally, cancer has become second leading cause of death, the number of cancer-related death was reported to be 8.8 million in 2015.[1,2] In China, it was also reported that 10,000 patients were diagnosed as cancer every day.[2] In terms of gender, the incidence of cancer in men is 61% higher than that in women, and the relative incidence index is 1.61 times.[2,3] 15% of male patients are younger than 55 years old, and about a quarter of them are younger than 20 years old.[4]

However, with the development of the treatment level for tumor diseases, the survival time of patients with cancer is significantly prolonged. A report published in 2016 indicated that 5-year survival rate for people diagnosed with cancer were around 69%.[2] Therefore, the current emphasis is not only the survival, but also the quality of life, especially it is crucial for men who are unmarried, maintaining fertility.

Ferlay et al reported that some tumor patients have azoospermia before treatment, indicating that the tumor itself might be one of the pathogenic factors of azoospermia.[5] In addition, the damage of fertility caused by radiotherapy and chemotherapy is well known.[5] This is because that testicular tissue is very sensitive to radiotherapy and some drugs such as alkylating agents and platinum clearly have a destructive effect on testicular tissue.[6] Although damage to male fertility by tumor itself, and chemo-radiotherapy/targeted therapy is clear, people's awareness of fertility preservation (FP) is insufficient, especially in China.[7–9] The main reason may be contributed to that both medical staffs and patients have no enough knowledge and correct attitude about FP.

During the antitumor treatment period, medical staff, especially nursing staff, should focus on the patient's long-term quality of life and health education. However, at the physician's level, many reports indicated that physicians have a lower response rate to FP. In a national survey, the response rates of physicians from United States, UK, and Japan were 15%, 37.6%, and 52%, respectively.[10] For cancer patients, some patients concerned about the cost of sperm storage, and more patients worried about whether cryopreservation would affect their offspring and whether cryopreservation would have an impact on genetics or deoxyribonucleic acid (DNA).

Nowadays, there is an increasing topic about the FP and the safety of sperm cryopreservation. Epidemiological surveys have found that hereditary tumors account for less than 1% of all tumors,[11] and a few families with hereditary tumors can achieve the desire to have healthy children through freezing techniques.[12]

Therefore, the purpose of the present study is to investigate the status of knowledge level and cognitive attitude of patients and medical staffs on FP and compare the sperm quality before and after radiotherapy/chemotherapy and before and after sperm cryotherapy. Thus, to make medical staff and patients have a clearer understanding of the importance and safety of sperm cryotherapy for FP in young male patients with cancer.

2. Materials and methods

2.1. Study population

First, according to another series of studies by our research team, we investigate the status of the knowledge level and attitudes on FP by surveying 332 cancer patients and 103 medical staff with questionnaires. Second, we selected 30 patients with malignant tumors who were diagnosed at the Sichuan Cancer Hospital from January 2018 to August 2018 as an experimental group. Thirty medical staffs and 30 cancer patients were also surveyed, the scores of the knowledge level, attitudes and behaviors were compared between medical staffs and cancer patients.

The selection of the patients was performed according to the following criteria:

(1) patients aged 16 to 45 years,
(2) patients with expected survival time ≥1 year and
(3) patients with expected completion of more than 3 radiotherapy program and/or chemotherapy cycles.

The average age of the 30 patients was 28 years, in which 20% of patients had child and 14% had been married. At the same time, we selected 30 age-, family status- and marriage-matched healthy men as a control group. The general information of the patients and the healthy controls was shown in Table 1.

Physicians and cancer patients were respectively obliged to respond to 9 and 8 statements to demonstrate their knowledge of the effect of cancer treatments on fertility, or about FP. Each question with the right answer or a positive statement (ie, "I Know" or "Yes") was scored as 1 point; otherwise, answers were scored as 0 point. As for FP attitudes, all response options to the items were on a 3-point Likert scale. One item was used to assess the degree of patient and physician's level of attention given FP (ie, not concerned to very concerned). Each option of each item was scored from 1 to 3, and the total possible overall attitude score was 15 points. Additionally, 8 items were used to evaluate practice behaviors on a 5-point Likert scale (never to always).

The study was approved by the Ethics Committee of Sichuan Cancer Hospital and all patients signed informed consent.

2.2. Autologous sperm preservation

First, we explained the process and precautions of the autologous sperm preservation to cancer patients and normal subjects. Second, the subjects signed the agreement and relevant information was registered into sperm bank system. Third, patient and normal subjects collected the semen by self-masturbation.

Afterward, we checked the sperm sample DNA fragmentation index by using sperm DNA fragmentation (SDF) staining Kit (Anhui Anke Biotechnology (Group) Co Ltd, China). Meanwhile, we performed the semen analysis including sperm concentration, progressive sperm motility (PR), mycoplasma culture, chlamydia culture, aerobic culture, and gonococcal culture by using Olympus CX41 phase contrast microscope, sperm counting board (Sefi-Medical Instrument, Israel), MyCoplasma IES Test kit (Zhuhai DL Biotech Co, Ltd, Guangdong, P. R. China), blood agar and chocolate agar.

Table 1

Tumor types and more information about the different cancer types in those 30 patients can be founded.

Diseases	n	Sperm quality C (mL)	Sperm quality PR (%)	C after treatment (mL)	PR after treatment (%)	Sperm condition after centrifugation	Chemotherapy Drugs	Chemotherapy Dose (mg)	Chemotherapy Cycle	Targeted treatment Drugs	Targeted treatment Dose (mg)	Targeted treatment Cycle	Radiotherapy Site	Radiotherapy dose (CGY)	Average dose (CGY)	Frequency
Nasopharyngeal carcinoma	10	104	37	0	0	No sperm after centrifugation	T	180	3	Nimotuzumab	200	6	Nasopharyngeal	7400	236,800	32
							P	30								
Nasopharyngeal carcinoma		65	64	0	0	No sperm after centrifugation	T	240	2	-			-			
							P	40								
							Xeloda (Capecitabine)	500								
Nasopharyngeal carcinoma		49	62	0	0	No sperm after centrifugation	T	240	5	Nimotuzumab	200	6	GTVnx, GTVLnL	7192	213,248	32
													GTVnR	7164		
							P	40					CTVI	6512		
													CTV2	5788		
Nasopharyngeal carcinoma		56	46	0	0	No sperm after centrifugation	T	240	4	Nimotuzumab	200	5	Nasopharyngeal	7200	422,400	32
							P	40					Benign part of the lymph	7000		30
													Lymphatic drainage area	5800		
Nasopharyngeal carcinoma		53	47	0.4	0	All D grade sperm	T	210	1	-			Nasopharyngeal	7400	236,800	32
							P	30								
							Docetaxel	100	4							
							P	40								
Nasopharyngeal carcinoma		36	51	0.1	0	All D grade sperm	T	210	4	Nimotuzumab	200	12	Nasopharyngeal	7580	213,708	33
													Lymph node metastasis	7500		
													High-risk subclinical lesion	6600		
							Nedaplatin	120					Low subclinical lesion	5600		
													Bilateral cervical lymph nodes	5100		
Nasopharyngeal carcinoma		110	66	0.1	0	All D grade sperm	T 1-d	210	1	Nimotuzumab	200	8	GTV	7400	318,200	33
							DDP 3-d	40					GTVln	7000		
							DDP 3-d	40					CTV1	6600		
							Loplatin	50					CTV2	6000		
							T	210					CTVln	5000		28
							Loplatin	50								
Nasopharyngeal carcinoma		39	65	0.2	0	Most of the B grade sperm	T	210	5	-			GTV	7000	219,450	33
													GTV 1n	7000		
							P	40					CTV1	6600		
													CTV2	6000		
Nasopharyngeal carcinoma		23	62	0	0	No sperm after centrifugation	T	240	4	-			Nasopharyngeal	7000	219,450	31
							P	50					Benign part of the lymph	6200		6
													Lymphatic drainage area	5500		25
Nasopharyngeal carcinoma		32	37	0	0	No sperm after centrifugation	T	220	2	-			GTV	7330	223,905	33
							P	50					GTV 1n	7280		33
							P	220	3				CTV1	6530		33
							Loplatin	50					CTV2	6000		33
													CTV 1n	5000	140,000	28
Lymphoma	5	47	53	0	0	No sperm after centrifugation	R 1-day	700		-			-			

(*continued*)

Table 1
(continued).

Diseases	n	Sperm quality: C (mL)	PR (%)	C after treatment (mL)	PR after treatment (%)	Sperm condition after centrifugation	Chemotherapy: Drugs	Dose (mg)	Cycle	Targeted treatment: Drugs	Dose (mg)	Cycle	Radiotherapy: Site	Radiotherapy dose (CGY)	Average dose (CGY)	Frequency
							VDS 1-d	4								
							CTX 1-d	1400								
Lymphoma		10	46	0	0	No sperm after centrifugation	Epirubicin	80	6	-			-			
							Bleomycin	15								
							VDS	4								
							Dacarbazine	600								
Lymphoma		50	50	0	0	Only 1 D grade sperm	R-CVP		3	-			-			
							R-CHOP		5							
Hodgkin lymphoma		29	41	0	0	No sperm after centrifugation	Epirubicin	60	6	-			-			
							Bleomycin	15								
							VDS	4								
							Dacarbazine	600								
Hodgkin lymphoma		86	73	0	0	No sperm after centrifugation	Epirubicin	40	6	-			-			
							Bleomycin	15								
							VDS	4								
							Dacarbazine	600								
Testicular tumor	4	19	52	0	0	No sperm after centrifugation	P	40	6	-			-			
							VP16	100								
Testicular tumor		64	30	6.5	0	All D grade sperm	P	30	2	-			-			
							VP16	100								
							Bleomycin	30								
Mediastinal germ cell tumor		26	56	0	0	No sperm after centrifugation	Cisplatin	40	3	-			-			
							Etoposide	100								
Testicular tumor		37	53	0	0	No sperm after centrifugation	Etoposide	120	2	-			-			
							P	30								
Glioma	2	11.6	60	4.9	70		Oxo Po	100	6	-			Intracranial	6000	180,000	30
Glioma		33	24	58	30					-			PGTV	5092	145,488	28
													PGTVtb	5400		
													PTV	5096		
Fibrosarcoma	3	25	50	44	41					-			Left thigh	6000	180,000	30
Soft tissue sarcoma		55	25	52	33					-			PCTV1	6250	292,500	26
													PGTV-nd	5000		
Mucinous liposarcoma		99	65	0	0	No sperm after centrifugation	Sample shedding									
Acinar cell carcinoma	2	44	75	50	78								Head and neck	6600	19,800	30
Parotid acinar cell carcinoma		141	44	0.8	25		PTX-SLN	240	2				Head and neck	7000	192,000	32
							Loplatin	90					Tumor bed	6000		
													Lymphatic	5000		
Spermato cell tumor	1	37	53	0	0	No sperm after centrifugation	Etoposide	120	2							
							P	30								
Schwannoma	1	0.4	*	0.4	0	Most of the AB grade sperm	Isophosphamide		6					175		35
							Epirubicin									
							Dacarbazine									
							Mesna									
Right ethmoid sinus malignancy	1	35	33	0	0	No sperm after centrifugation	Sample shedding									
Acute lymphoblastic leukemia	1	15	75	0	0	No sperm after centrifugation	R-CVP		3							
							R-CHOP		5							

C = concentration, PR = progressive sperm motility.
* occasionally ABC grade, the rest is D grade sperm.

4443-

Sterile CBS^{TM} high security tube (Cryo Bio System), sealer (Cryo Bio System SYMSIII) and cryoprotective solution (Self-prepared yolk-free modified Tyrode solution) were used for sperm freezing. The procedure of sperm freezing was as follow:

(1) the cryoprotectant and semen were added to the cryotube at a ratio of 1:3 and mixed, 1 mL per tube,
(2) the mixed semen samples were placed at 4°C for 15 minutes, and then placed 5 cm above the liquid nitrogen for 10 minutes, and
(3) placed in liquid nitrogen in an Isothermal Liquid Nitrogen Freezers (CBS, V1500AB).

When sperm were needed, the sample was taken out from the liquid nitrogen and placed at room temperature for 2 minutes, and then placed in a 37°C water bath for re-warming. The sample should be gently inverted and mixed, and then the sperm concentration, PR and SDF index after cryopreservation were analyzed.

2.3. Self-prepared yolk-free modified Tyrode solution

The self-prepared yolk-free modified Tyrode solution is a human sperm freezing protection solution containing no egg yolk and includes the following components and the final concentration of each component for sperm cryopreservation is: sodium chloride 90 to 110 mmol/L, Potassium chloride 5 to 6 mmol/L, magnesium sulfate 0.2 to 0.5 mmol/L, calcium chloride 2 to 4 mmol/L, sodium dihydrogen phosphate 0.2 to 0.5 mmol/L, sodium hydrogencarbonate 28 to 35 mmol/L, glycine 110 to 150 mmol/L, 4-hydroxyethylpiperazineethanesulfonic acid 18 to 25mmol/L, glucose 5 to 8 mmol/L, sucrose 30 to 60 mmol/L, sodium lactate 12 to 15 mmol/L, glycerol 50 to 100 mL/L, balance for ultra pure water. Since the solution does not contain egg yolk, it is not easy to cause an allergic reaction. The self-prepared yolk-free modified Tyrode solution is the patent we applied for (http://epub.sipo.gov.cn/patentoutline.action, Patent No: 2017103753849). It has a good protective effect on the freezing injury during sperm freezing and has no obvious negative impact on sperm physiological function, so it has good PR and recovery rate after sperm after resuscitation.

2.4. Evaluation

According to the requirements of the World Health Organization laboratory manual for the examination and processing of human semen (5th Edition),[13] Sperm concentration, PR and DNA fragmentation index were 3 key indicators to evaluate the sperm quality. At least 200 sperms were calculated by Computer-aided sperm analysis (Beijing Suijia Software Co, Ltd. Beijing, P.R. China) to PR and repeated the detection twice. If the difference in test results is acceptable we will take the mean value or repeat the test twice if it is not acceptable.

SDF was defined as single or double strand breaks in nuclear DNA resulting in a potential loss/alteration of genetic information; sperm DNA integrity can be detected by sperm chromatin structure assay detects.[14] Many genotoxic experiments showed excellent dose response data with very low coefficient of variation that further validated the sperm chromatin structure assay as being a highly powerful assay for sperm DNA integrity.[14] The slide containing the semen sample was subjected to steps of dissolving, cooling, staining and rinsing, then researchers observed the results under a normal light microscope ($40 \times 10 \times$ field of view), count at least 500 sperm and calculate the percentage of abnormal sperm.

Judging criteria for normal sperm and abnormal sperm: large halo and middle halo are normal sperm; small halo, no halo and degenerate sperm are abnormal sperm. Halo width/sperm head diameter $\geq$2/3 for large halo; 1/4 $<$ halo width/sperm head diameter $<$2/3 for the halo ring; halo width/ sperm head diameter $\leq$1/4 for small halo Ring; no halo is observed as halo-free; spermatozoa in the sperm nuclei is degraded sperm.

2.5. Statistical methods

All analyses were conducted using SPSS Windows package (version 16.0, SPSS, Inc, Evanston, IL). Student t test was used compare the sperm concentrations and PR between normal controls and tumor patients. Paired sample T test and Z test were used to analyze the effects of antitumor therapy and sperm cryopreservation on sperm quality and sperm DNA fragments. A $P < .05$ was considered to be statistically significant.

3. Results

3.1. The trend of sperm quality and antitumor treatment

Table 1 illustrated the tumor types and more information about the different cancer types in those 30 patients can be founded.

3.2. Knowledge level and cognitive attitude of patients and medical staff on FP

According to another series of studies by our research team, as can be seen from a survey of 332 cancer patients,[15] 77.8% of patients realized that tumors and their treatment would damage fertility, 27.7% of patients worried that tumors would affect the DNA of offspring, but 71.1% of patients still do not know the existence of sperm banks. Additionally, the knowledge of FP by medical staff was also limited. From the survey of 103 medical staff, 73.8% of medical staff did not consult the reproductive experts about fertility preservation, and 84.5% of medical staff did not even receive any knowledge of FP.

During the process of previous study, we compared the knowledge level, cognitive attitudes and practice behaviors of FP between 30 medical staffs and 30 cancer patients. The scores (mean $\pm$ standard deviation) of knowledge level and cognitive attitude on the patient's FP in medical staffs were 3.91 ± 1.67 and 12.29 ± 1.23, respectively. The scores in the patients were 3.50 ± 0.70 and 10.33 ± 0.95, respectively. These scores were relatively low when compared to full scores of knowledge level (8 points) and cognitive attitude (15 points). In addition, in the absence of knowledge and attitude, the practice of FP by medical staff and patients was 30.1% and 6.67%, respectively.

3.3. Effects of tumors and radiotherapy/chemotherapy on antitumor therapy on sperm quality

As shown in Table 2, the mean, SD and median of sperm concentration in patients with tumor before antitumor treatment were lower than those in normal subjects ($P = .010$). Compared to normal donors, the DNA fragments of tumor patients were significantly more ($P = .0001$).

After anti-tumor treatment, 25 cases of the 30 patients continued to perform sperm quality testing. No sperm was detected after centrifugation in 11 cases, and D-class sperm was detected in 6 cases. Additionally, the sperm concentration and PR

Table 2

Comparison of semen analysis between cancer patients and normal sperm donors.

	n	Sperm concentration ($\bar{x} \pm s$)	Sperm concentration (Median)	PR (Median)	Z	P
Normal patients	30	94.53±69.89	80	67.5	−2.571	.01
Cancer Patients	30	56.02±32.57	51.5	51		

PR = progressive sperm motility.

Table 3

Comparison of sperm analysis before cryopreservation and after antitumor treatment in cancer patients.

	n	Sperm concentration ($\bar{x} \pm s$)	Sperm concentration (median)	PR ($\bar{x} \pm s$)	PR (median)
Before cryopreservation	25	56.02±32.57	51.5	51.30±14.15	51
After cryopreservation	25	10.67±20.27*	0.10*	13.32±24.12†	0.00†

PR = progressive sperm motility.
Compared with sperm corn before cryopreservation; *: $Z=-3.929$, $P=.000 < .01$.
Compared with sperm corn before cryopreservation; †: $Z=-4.077$, $P=.000 < .01$.

of the tumor patients after treatment were lower than those of the tumor patients before treatment (all $P=.001$) (Table 3).

3.4. The effect of sperm cryopreservation on sperm quality and DNA fragment integrity

The sperm concentration and PR after the sperm cryopreservation were significantly lower than that before cryopreservation in both cancer patient and normal donors (all $P=.0001$, Table 4).

Compared with the DNA fragments of spermatozoa before cryopreservation, the DNA fragments after cryopreservation were slightly more but did not reach statistically significant in both groups ($P=.829$) (Table 5).

4. Discussion

The impact of tumor itself on sperm quality has been well documented.[16] Auger et al demonstrated that various types of tumors can have a series of effects on sperm quality in young tumor patients when compared the sperm quality between 4480 young cancer patients and 1148 healthy sperm donors.[17] Williams et al showed that testicular tumors may reduce the sperm quality by directly damaging germ cells[18] and van Casteren et al revealed that other types of malignant tumors such as leukemia, lymphoma, and gastrointestinal tract increase the risk of azoospermia in men.[19] In addition, some patients with tumors have had azoospermia before treatment, which fully indicates that the tumor itself is one of the pathogenic factors of azoospermia.[5] The present study showed that sperm concentration and/or PR in tumor patients were significantly lower while sperm DNA fragments were significantly more in cancer patients than those in normal donors, that are consistent with the findings of other studies described above. This study was also help newly diagnosed young male cancer patients make important decisions such as to pursue cryopreservation before undergoing treatment.

Here, the most important point we should emphasized is that antitumor treatment such as radiotherapy and/or chemotherapy

Table 4

Comparison of sperm quality before and after cryopreservation in patients with cancer.

	n	Sperm concentration ($\bar{x} \pm s$)	Sperm concentration (median)	PR ($\bar{x} \pm s$)	PR (median)
Before cryopreservation	30	56.02±32.57	51.5	51.30±14.15	51
After cryopreservation	30	38.13±26.99*	31.5*	31.13±12.73†	29.5†

PR = progressive sperm motility.
Compared with sperm corn before cryopreservation; *: $Z=-4.785$, $P=.000 < .01$.
Compared with sperm corn before cryopreservation; †: $Z=-4.786$, $P=.000 < .01$.
*,† $P<.05$ versus sperm corn before cryopreservation.

Table 5

Comparison of DNA fragment index (%) among normal patients, tumor patients before and after cryopreservation.

	n	DNA fragmentation index ($\bar{x} \pm s$)	DNA fragmentation index (Median)	Z	P
Normal patients	30	12.97±7.06	11.00		
Before cryopreservation (CP)	30	33.43±21.79†	28.00†	−4.310	.000
After cryopreservation (CP)	30	33.70±19.50*	29.00*	−0.217	.829

CP = cancer patients.
Compared with cancer patients (before cryopreservation); *: $Z=-0.217$, $P=.829$; $P>.05$ versus cancer patients (before cryopreservation).
Compared with normal patients; †: $Z=-4.310$, $P=.000$; $P<.05$ versus normal patients.

would further damage the sperm quality in these patients.[5] This is because that testicular tissue is extremely sensitive to radiotherapy and has a clear dose-related, and most chemotherapeutic drugs have reproductive toxicity.[20] In addition, other treatment options for tumors such as surgery and targeted therapy could also lead to a decline in male fertility.[21]

In the present study, we also showed that azoospermia or low-class sperm occurred in more than 60% of tumor patients after antitumor therapies. Therefore, autologous sperm cryopreservation is necessary before treatment for the patients who wish to preserve their fertility.

Although sperm quality is damaged by tumor itself, it is believed that cryopreservative sperm from cancer patients before treatment can be used in In Vitro Fertilization- Intracytoplasmic Sperm Injection programs.[22] A number of success cases to father their genetic children have been reported.[23] In addition, it is worth mentioning that the emergence of (intra cytoplasmic sperm injection) technology allows a small number of viable sperm to complete the conception process. This greatly reduces the need for sperm quality and indicates the importance of semen preservation, enabling more patients to obtain fertility opportunities from autologous semen preservation. However, it needs to follow-up to observe whether the cryopreservative sperm of the 30 cancer patients in the present study can create babies in the future studies.

Concerning effect of cryopreservation on sperm quality, it has been reported that cryopreservation can reduce sperm motility, but did not influence the potential fertility by analyzing the semen parameters in 14 years of cryopreservative semen samples[19] and some researchers believe that long-term cryopreservation had better safety, effectiveness and recovery rate.[24] Furthermore, according to the World Health Organization laboratory manual for the examination and processing of human semen, the lower limit of the reference value of sperm concentration is 12 to 16, and the lower limit of reference value of PR is 31 to 34.[25] In the present study, the mean of sperm concentration and PR after freezing were 38.13 and 31.13, respectively that are close to the reference values, which may be enough to satisfy artificial fertility[25] although sperm quality was reduced after cryopreservation.

DNA fragment index is an indicator for sperm integrate and a novel marker for sperm fertility.[26] Some studies pointed out that the reasons for parents to give up sperm freezing include the safety of pregnancy, or the genetic risk of malignant tumors.[27] However, in the present study, we showed that there was no significant difference in DNA fragment index before and after freezing, suggesting that the freezing technique is safe and reliable and does not affect the patient's genetic function.

In addition to a clear genetic syndrome, there is no evidence that tumor itself, anti-tumor treatment or fertility intervention may increase the risk of cancer or congenital malformations in future generations.[1]

China's fertility protection technology is carried out far later than developed countries. Although sperm freezing is a reproductive benefit for cancer patients, especially unmarried young men, only small number of participants join the program. At present, there is a lack of research on fertility protection provided by oncologists in China, and the lack of information on sperm freezing in cancer patients is still a common phenomenon in society.

In conclusion, the present study demonstrated that tumor treatment can further damage the sperm quality in addition to tumor itself. Therefore, sperm freezing is very necessary in young cancer patients, and the freezing time is best before anti-tumor treatment. We also demonstrated that the cryopreservation did not significantly affect the sperm integrate and fertility potential. However, the majority of physicians and cancer patients lack the knowledge and the correct attitude about sperm cryopreservation for male FP. The National Comprehensive Cancer Network Guidelines for Adolescents and Young Patients with Malignant Tumors suggest that physicians should communicate treatment-related reproductive toxicity and fertility protection measures with patients and their families before treatment, and recommend reproductive specialists for patients with fertility needs.[27] Therefore, it is the responsibility for physician to advise the tumor patient to perform sperm cryopreservation before treatment, and to inform the patient of the benefits of cryopreservation, to eliminate the patient's concerns that sperm freezing may affect the DNA of his offspring, and to achieve reproductive benefit for young male patients.

5. Limitation and future implications

The sample size of this study was small and included different types of tumor. The sperm analysis of 5 patients was not collected after anti-tumor treatment. However, as this study is a continuous research, follow-up work on patients after treatment is ongoing, and sperm analysis after treatment is still collecting. Future research can expand the sample size, focus on the single disease, and analyze the relationship between different diseases in male sperm quality and fertility. In addition, future research should also focus on DNA damage and chromosomal aberrations, embryonic development abnormalities, and birth defects.

Acknowledgment

The authors would like to thank the staff in the department of human sperm bank, who helped in collecting data. Many thanks to Professor Guorong Wang for her advice on data statistics and the handling of SPSS. We also would like to thank the Scientific Research of Sichuan Province Health Department for the financial support.

Author contributions

Conceptualization: Yinfeng Li, Jian Zhang, Hanfeng Zhang, Lin Yu, Xiaohui Jiang.
Data curation: Yinfeng Li, Bencui Fu, Yang Xian, Bizhen Su.
Formal analysis: Yinfeng Li, Maoqiu Cao, Hui Li.
Funding acquisition: Jian Zhang.
Methodology: Hanfeng Zhang.
Project administration: Bo Liu, Guorong Wang, Maoqiu Cao, Xiaohui Jiang.
Resources: Bo Liu, Bencui Fu, Lin Yu.
Software: Guorong Wang.
Supervision: Hanfeng Zhang, Guorong Wang, Maoqiu Cao, Qinghua Jiang, Lin Yu, Yang Xian, Bizhen Su.
Validation: Bencui Fu, Qinghua Jiang.
Visualization: Hui Li, Qinghua Jiang.
Writing – original draft: Yinfeng Li.
Writing – review and editing: Yinfeng Li, Xiaohui Jiang.

References

[1] Byrne J, Rasmussen SC, Steinhorn RR, et al. Genetic disease in offspring of long-term survivors of childhood and adolescent cancer. Am J of Hum Genet 1998;62:45–52.

[2] WHO. (2018). Available at: http://www.who.int/mediacentre/factsheets/fs297/en/. Accessed 16 August 1998.
[3] Polland A, Berookhim BM. Fertility concerns in men with genitourinary malignancies: treatment dilemmas, fertility options, and medicolegal considerations. Urol Oncol 2016;34:399–406.
[4] Heyu P, Rongfshou Z, Xibing S, et al. Analysis of gender differences in malignant tumors in China. J China Cancer 2013;22:174–9.
[5] Ferlay J, Steliarova-Foucher E, Lortet-Tieulent J, et al. Cancer incidence and mortality patterns in Europe: estimates for 40 countries in 2012. Eur J Cancer 2013;49:1374–403.
[6] Xiaohua L, Jiabao W, Yunge T. Effect of tumor and its treatment on fertility of male patients and genetic risk analysis. Chin J Fam Plan 2018;26:415–9.
[7] Trost LW, Brannigan RE. Oncofertility and the male cancer patient. Curr Treat Options Oncol 2012;13:146–60.
[8] Hallak J, Mahran AM, Agarwal A. Characteristics of cryopreserved semen from men with lymphoma. J Assisted Reprod Genet 2000;17:591–5.
[9] Centola GM, Keller JW, Henzler M, et al. Effect of low-dose testicular irradiation on sperm count and fertility in patients with testicular seminoma. J Androl 1994;15:608–13.
[10] Ronquist G, Brody I. The prostasome: its secretion and function in man. Biochim Biophys Acta 1985;822:203–18.
[11] Pacey AA, Merrick H, Arden-Close E, et al. Monitoring fertility (semen analysis) by cancer survivors who banked sperm prior to cancer treatment. Hum Reprod 2012;27:3132–9.
[12] Burrell RA, McGranahan N, Bartek J, et al. The causes and consequences of genetic heterogeneity in cancer evolution. Nature 2013;501:338–45.
[13] Xingwu C, Kai L, Cuiying L. A review of WHO laboratory manual for the examination and processing of human semen(5th edition). National Journal of Andrology 2011; 17: 1059-1063.
[14] Donald PE. The sperm chromatin structure assay (SCSA®) and other sperm DNA fragmentation tests for evaluation of sperm nuclear DNA integrity as related to fertility. Anim Reprod Sci 2016;169:56–75.
[15] Zhang H, Wang G, Jiang B, et al. The knowledge, attitude, and self-reported behaviors of oncology physicians regarding fertility preservation in adult cancer patients. J Cancer Educ 2019;doi: 10.1007/s13187-019-01567-6.
[16] de Pedro M, Otero B, Martin B. Fertility preservation and breast cancer: a review. Ecancermedicalscience 2015;9:503–23.
[17] Auger J, Sermondade N, Eustache F. Semen quality of 4480 young cancer and systemic disease patients: baseline data and clinical considerations. Basic Clin Androl 2016;26:3–13.
[18] Williams IV DH, Karpman E, Sander JC, et al. Pretreatment semen parameters in men with cancer. J Urol 2009;181:736–40.
[19] van Casteren NJ, Boellaard WP, Romijn JC, et al. Gonadal dysfunction in male cancer patients before cytotoxic treatment. Int J Androl 2010; 33:73–9.
[20] Wyrobek AJ. Relative susceptibilities of male germ cells to genetic defects induced by cancer chemotherapies. J Natl Cancer Inst Monogr 2005; 34:31–5.
[21] Smith GD, Serafini PC, Fioravanti J, et al. Prospective randomized comparison of human oocyte cryopreservation with slow-rate freezing or vitrification. Fertil Steril 2010;94:2088–95.
[22] Sheng HQ, Zhang XZ, Hong Y. Analysis of the quality of cryopreserved semen from male cancer patients. Zhonghua Nan Ke Xue 2015;21:44–7.
[23] Katz DJ, Kolon TF, Feldman DR, et al. Fertility preservation strategies for male patients with cancer. Nat Rev Urol 2013;10:463–72.
[24] Yogev L, Kleiman SE, Shabtai E, et al. Long-term cryostorage of sperm in a human sperm bank does not damage progressive motility concentration. Hum Reprod 2010;25:1097–103.
[25] Ståhl O, Boyd HA, Giwercman A, et al. Risk of birth abnormalities in the offspring of men with a history of cancer: a cohort study using Danish and Swedish national registries. J Natl Cancer Inst 2011;103:398–406.
[26] Kort JD, Eisenberg ML, Millheiser LS, et al. Fertility issues in cancer survivorship. CA Cancer J Clin 2014;64:118–34.
[27] Lawson AK, Klock SC, Pavone ME, et al. Psychological counseling of female fertility preservation patients. J Psychosoc Oncol 2015;33:333–53.

日中笹川医学奨学金制度(学位取得コース)評価書
課程博士：指導教官用

第 41 期　研究者番号： G4110　作成日 ： 2021 年 1 月 12 日

氏　名	崔　力萌	CUI　LIMENG	性別	F	生年月日　1986. 11. 03
所属機関（役職）	北京市予防医学研究センター放射衛生防護所（職員）				
研究先（指導教官）	長崎大学原爆後障害医療研究所国際保健医療福祉学研究分野（高村 昇教授）				
研究テーマ	福島県富岡町における環境放射能モニタリングと住民の被ばく線量評価 Environmental monitoring and estimation of exposure doses of residents in Tomioka Town, Fukushima Prefecture				
専攻種別	☐論文博士	☑課程博士			

研究者評価（指導教官記入欄）

成績状況	(優)　良　可　不可 学業成績係数=	取得単位数 24／30
学生本人が行った研究の概要	長崎大学が復興推進拠点を設置している福島県富岡町の帰還困難区域において、除染を行って避難の解除を行う「特定復興再生拠点区域」とそれ以外の区域の空間線量率および放射性核種分析を経時的、面的に行った。その結果、特定復興再生拠点区域においては空間線量率が 2018 年から 2019 年の間で 1.0 マイクロシーベルト/時から 0.3 マイクロシーベルト/時と低下したのに対し、非除染地域は空間線量率の低下は限定的であった。また放射性セシウムが検出された地点は特定復興再生拠点区域では 64%から 6.7%に低下したのに対し、非除染地域は 93%から 88%とあまり低下していなかった。 以上のことから、富岡町における特定復興再生拠点区域での面的除染は有効であり、今後福島県下の他の自治体における特定復興再生拠点区域のモデルとなりうると考えられた。	
総合評価	【良かった点】 Cui Limeng は博士課程在学中に論文 3 編を執筆し、1 編は Scientific Reports に、あとの 2 編は PLoS One に掲載された。3 編のインパクトファクターの合計が 7 点を超えたため、早期修了（4 年間の博士課程を 3 年間で修了）の対象学生となった。 【改善すべき点】 特になし 【今後の展望】 今後は、本学での研究を踏まえ、放射線を含む環境科学分野において、政策提言につながるような研究を行うことが期待される。	
学位取得見込	2021 年 3 月に博士（医学）を取得予定	

評価者（指導教官名）　高村　昇　(印)

日中笹川医学奨学金制度(学位取得コース)報告書
研究者用

Supported by 日本財団 THE NIPPON FOUNDATION

第41期　　研究者番号： G4110　　作成日：2021年1月26日

氏名	Cui Limeng	崔 力萌	性別	F	生年月日 1986. 11. 03
所属機関(役職)	北京市予防医学研究中心（研究員）				
研究先（指導教官）	長崎大学原爆後障害医療研究所　国際保健医療福祉学研究分野（高村 昇教授）				
研究テーマ	福島県富岡町における環境放射能モニタリングと住民の被ばく線量評価 Environmental monitoring and estimation of exposure doses of residents in Tomioka Town, Fukushima Prefecture				
専攻種別	論文博士	☐	課程博士	☑	

1．研究概要（1）

1）目的（Goal）

Ascertain air dose rates and decontamination effect as well as analyses the radiocesium movement;
Determine the temporal evolution of the air dose rate in various land types;
Evaluate the effective dose for residents and workers.

2）戦略（Approach）

We carried out a detailed and high-frequency radiation monitoring program using a car-borne survey to provide relatively high-density data. We also evaluated the effects of decontamination efforts, such as reductions in ambient and radiocesium dose rates, in three areas (“Decontaminated area”, “Radioactive waste storage area” and “Non-decontaminated area”) with markedly different characteristics in the difficult-to-return zone in Tomioka Town.

3）材料と方法（Materials and methods）

We regularly measured the ambient dose rate from July 2018 to December 2019. The difficult-to-return zone of Tomioka Town was surveyed using a car-borne survey system, Radi-probe® (Model: HDS-101GN, Mirion Technologies, Inc., Japan). Combined with the output photos, the three districts were precisely divided. The measurement points ranged from 510 to 995, 747 to 1508 and 121 to 189 in the Radioactive waste storage area, Decontaminated area and Non-decontaminated area, respectively. Effective doses were determined for external exposure based on the following formula:

$$E_i = (D_{out} - D_{BG}) \cdot T \cdot R \quad \text{(a)}$$

$$E_w = \sum_{i=1}^{12} E_i \quad \text{(b)}$$

$$E = E_{out} + E_{in} \quad \text{(c)}$$

$$E_{out/in} = (D_{out/in} - D_{BG}) \cdot T \cdot F \cdot R \quad \text{(d)}$$

$$D_{in} = r \cdot D_{out} \quad \text{(e)}$$

where E_i is the estimated external effective dose (mSv/month by median); Ew is the external effective dose for decontamination workers (mSv/y); E is the external effective dose for residents who are going to return to the Decontaminated area (mSv/y); Eout/in is the external effective dose for outdoor and indoor workers; Dout/in is the dose rate for a height of 1 m above ground outside and inside the house (μSv/h); DBG is 0.04 μSv/h, which was measured in the area of interest before the accident40; T is the work time, 240 d × 8 h (normal labor standards in Japan); F is the occupancy factor1; R is the age-dependent dose conversion coefficient for adults (0.6), and, r is the deposited gamma location factor for a wooden house (0.4).

4）実験結果(Results)

The median dose rates in the “Decontaminated area” in the difficult-to-return zone decreased rapidly from 1.0 μSv/h to 0.32 μSv/h; however, the median dose rates in the “Non-decontaminated area” and “Radioactive waste storage area” were maintained between 1.1-1.4 μSv/h and 0.46-0.61 μSv/h, respectively. Ambient dose rates were significantly higher in the Non-decontaminated area than in the other two areas ($p < 0.001$). In the surveys during 2018 and on January 24, 2019, the dose rates in the Decontaminated area were significantly higher than those in Radioactive waste storage area ($p < 0.001$). However, in the survey on January 12, 2019 and the nine surveys after March 2019, the statistical results indicated the dose rates in the Decontaminated area fell below those of the Radioactive waste storage area ($p < 0.001$). We confirmed that the dose rates in the Decontaminated area dramatically decreased due to decontamination work aiming to help residents return home. Moreover, the estimated external exposure dose of workers during the present survey was 0.69 mSv/y in the Decontaminated area and 0.57 mSv/y in the Radioactive waste storage area, respectively. This case of Tomioka Town within the “difficult-to-return zone” may be the first reconstruction model for evaluating environmental contamination and radiation exposure dose rates due to artificial radionuclides derived from the nuclear disaster. The frequency distributions of the ambient dose rates within the difficult-to-return zone of Tomioka town were illustrated in Figure 1.

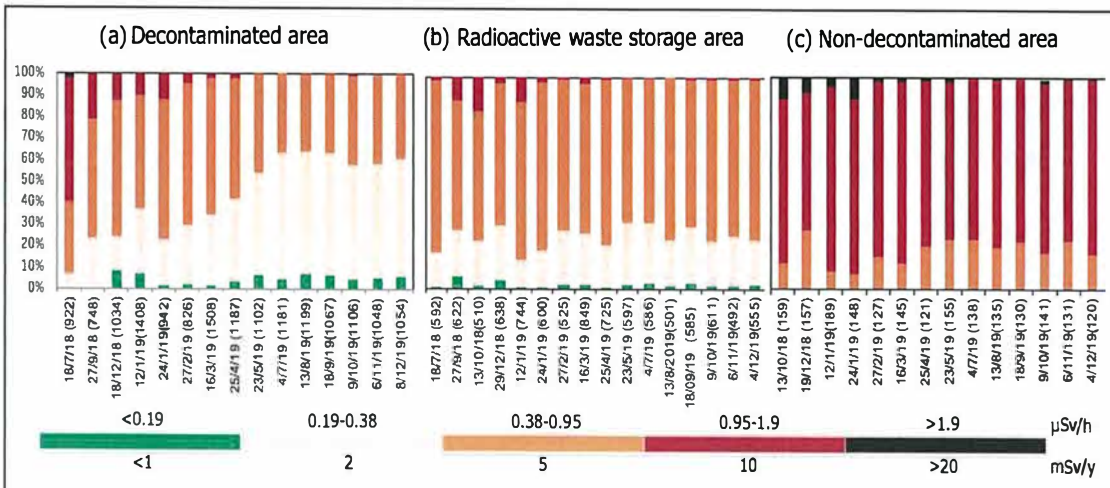

Figure 1. Relative frequencies of the ambient dose rates in difficult-to-return zone in Tomioka town, Fukushima prefecture during July 2018 to December 2019.

5）考察（Discussion）

The dose rates in the Decontaminated area decreased faster than those in the Radioactive waste storage area and Non-decontaminated area from July 2018 to December 2019. Significant differences in ambient dose rates were observed among surveys in the Decontaminated area, Radioactive waste storage area and Non-decontaminated area ($p<0.001$). Noticeable fluctuations in dose rates in the Radioactive waste storage area and Non-decontaminated area were observed. Also, a relatively stable downward trend was observed in the Decontaminated area. The main reason for the decrease in dose rates in Yonomori District is the decontamination efforts which have focused on removing deposits from roofs, decks and gutters; wiping off roofs and walls; high-pressure washing of houses and buildings; mowing lawns; removing fallen leaves and stripping topsoil in gardens; removing deposits in ditches and high-pressure washing of roads. Our results showed that the reduction rates of radiocesium in all three districts were noticeably faster than its physical decay. In the present study, the estimated annual effective dose of decontamination workers, as well as the residents of decontaminated areas, was lower than the annual effective dose limits recommended by the Japanese government. Nevertheless, radiation safety education for workers is needed to appropriately protect them from radiation. In conclusion, the long-term follow-up monitoring in combination with various analytical apparatus and system such as car-borne survey and nuclides analysis of the environmental samples could be accurately evaluate the decontamination effects, external and internal radiation levels. These monitoring is extremely important for the reconstruction of affected areas around the FDNPS.

6）参考文献（References）

1. Saito, K. & Petoussi-Henss, N. Ambient dose equivalent conversion coefficients for radionuclides exponentially distributed in the ground. J. Nucl. Sci. Technol. 51, 1274 - 1287 (2014).
2. Ministry of the Environment of Japan. Additional exposure doses after an accident (example of calculation). (Accessed August 23, 2019). https://www.env.go.jp/en/chemi/rhm/basic-info/1st/02-04-09.html (Accessed July 31, 2019) (2018).
3. Profes, E. et al. Nuclear power facilities such as disaster prevention measures consignment expenses (measurement of continuous air dose rate that simulated life action pattern) (in Japanese). (2017)
4. Ministry of the Environment of Japan. Shielding and reduction coefficient. (Accessed August 23, 2019). https://www.env.go.jp/en/chemi/rhm/basic-info/1st/02-04-08.html (Accessed July 31, 2019) (2018).
5. Ministry of health, labour and welfare, Japan. Guidelines on Prevention of Radiation Hazards for Workers Engaged in Decontamination Works. https://www.mhlw.go.jp/english/topics/2011eq/workers/ri/gn/gn_141118_a01.pdf (Accessed August 23, 2019).

2. 執筆論文　Publication of thesis　※記載した論文を添付してください。Attach all of the papers

論文名 1 Title	Chemical content and source apportionment of 36 heavy metal analysis and health risk assessment in aerosol of Beijing				
掲載誌名 Published journal	Environmental Science and Pollution Research				
	2019 年 12 月	27 巻（号）	7005 頁 ～ 7014 頁	言語 Language	English
第 1 著者名 First author	Limeng Cui	第 2 著者名 Second author	Zhuona Wu	第 3 著者名 Third author	Peng Han
その他著者名 Other authors	Yasuyuki Taira，Huan Wang，Qinghua Meng，Zechen Feng，Shuguang Zhai，Jun Yu，Weijie Zhu，Yuxia Kong，Hongfang Wang，Hong Zhang，Bin Bai，Yun Lou，Yongzhong Ma				
論文名 2 Title	日本福岛第一核电站事故七年后环境放射性水平与公众健康情况的现状及启示 Situation and enlightenment in an environmental radioactivity and public health perspective seven years after Fukushima nuclear power plant accident				
掲載誌名 Published journal	中华放射医学与防护 Chinese Journal of Radiological Medicine and Protection				
	2019 年 8 月	39（8） 巻（号）	619 頁 ～ 623 頁	言語 Language	Chinese
第 1 著者名 First author	崔力萌	第 2 著者名 Second author	Noboru Takamura	第 3 著者名 Third author	马永忠
その他著者名 Other authors					
論文名 3 Title	Environmental Remediation of the difficult-to-return zone in Tomioka Town, Fukushima Prefecture				
掲載誌名 Published journal	Scientific Reports				
	2020 年 6 月	10 巻（号）	10165 頁 ～ 頁	言語 Language	English
第 1 著者名 First author	Limeng Cui	第 2 著者名 Second author	Yasuyuki Taira	第 3 著者名 Third author	Masahiko Matsuo
その他著者名 Other authors	Makiko Orita, Yumiko Yamada, Noboru Takamura				
論文名 4 Title	Radiocesium concentrations in wild boars captured within 20 km of the Fukushima Daiichi Nuclear Power Plant				
掲載誌名 Published journal	Scientific Reports				
	2020 年 6 月	10 巻（号）	9272 頁 ～ 頁	言語 Language	English
第 1 著者名 First author	Limeng Cui	第 2 著者名 Second author	Makiko Orita	第 3 著者名 Third author	Yasuyuki Taira
その他著者名 Other authors	Noboru Takamura				
論文名 5 Title					
掲載誌名 Published journal					
	年 月	巻（号）	頁 ～ 頁	言語 Language	English
第 1 著者名 First author		第 2 著者名 Second author		第 3 著者名 Third author	
その他著者名 Other authors					

3. 学会発表 Conference presentation ※筆頭演者として総会・国際学会を含む主な学会で発表したものを訁

※Describe your presentation as the principal presenter in major academic meetings including general meetings

学会名 Conference	日本放射線影響学会第62回大会
演 題 Topic	Environmental Remediation of a Restricted Area in Tomioka Town, Fukushima Prefecture
開催日 date	2019 年 11 月 16 日 開催地 venue 京都大学
形式 method	☐ 口頭発表 Oral ☑ ポスター発表 Post 言語 Language ☐ 日本語 ☑ 英語 ☐ 中国語
共同演者名 Co-presenter	Limeng Cui, Yasuyuki taira, Masahiko Matsuo, Makiko orita, Yumiko Yamada, Noboru Takamura
学会名 Conference	ICRP International Conference on Recovery After Nuclear Accidents
演 題 Topic	Environmental Remediation of the difficult-to-return zone in Tomioka Town, Fukushima Prefecture
開催日 date	2020 年 12 月 1 日 開催地 venue Zoom
形式 method	☐ 口頭発表 Oral ☑ ポスター発表 Post 言語 Language ☐ 日本語 ☑ 英語 ☐ 中国語
共同演者名 Co-presenter	Limeng Cui, Yasuyuki taira, Masahiko Matsuo, Makiko orita, Yumiko Yamada, Noboru Takamura
学会名 Conference	The 5th International Symposium of the Network-type Joint Usage/Research Center for Radiation Disaster Medical Science
演 題 Topic	Environmental Remediation of the difficult-to-return zone in Tomioka Town, Fukushima Prefecture
開催日 date	2021 年 2 月 8 日 開催地 venue Zoom
形式 method	☐ 口頭発表 Oral ☑ ポスター発表 Post 言語 Language ☐ 日本語 ☑ 英語 ☐ 中国語
共同演者名 Co-presenter	
学会名 Conference	
演 題 Topic	
開催日 date	年 月 日 開催地 venue
形式 method	☐ 口頭発表 Oral ☐ ポスター発表 Post 言語 Language ☐ 日本語 ☐ 英語 ☐ 中国語
共同演者名 Co-presenter	

4. 受賞（研究業績Award (Research achievement)

名 称 Award name				
	国名 Country		受賞年 Year of	年 月
名 称 Award name				
	国名 Country		受賞年 Year of	年 月

5. 本研究テーマに関わる他の研究助成金受給 Other research grants concerned with your resarch theme

受給実績 Receipt record	■ 有　□ 無
助成機関名称 Funding agency	Ministry of the Environment, Japan
助成金名称 Grant name	Research on the Health Effects of Radiation
受給期間 Supported period	年　月 ～　年　月
受給額 Amount received	円
受給実績 Receipt record	□ 有　□ 無
助成機関名称 Funding agency	
助成金名称 Grant name	
受給期間 Supported period	年　月 ～　年　月
受給額 Amount received	円

6. 他の奨学金受給 Another awarded scholarship

受給実績 Receipt record	□ 有　□ 無
助成機関名称 Funding agency	
奨学金名称 Scholarship name	
受給期間 Supported period	年　月 ～　年　月
受給額 Amount received	円

7. 研究活動に関する報道発表 Press release concerned with your research activities

※記載した記事を添付してください。Attach a copy of the article described below

報道発表 Press release	□ 有　■ 無	発表年月日 Date of release	
発表機関 Released medium			
発表形式 Release method	・新聞　・雑誌　・Web site　・記者発表　・その他(　　　)		
発表タイトル Released title			

8. 本研究テーマに関する特許出願予定 Patent application concerned with your research theme

出願予定 Scheduled	□ 有　■ 無	出願国 Application	
出願内容(概要) Application contents			

9. その他 Others

指導責任者(署名)

Chemical content and source apportionment of 36 heavy metal analysis and health risk assessment in aerosol of Beijing

Limeng Cui, Zhuona Wu, Peng Han, Yasuyuki Taira, Huan Wang, Qinghua Meng, Zechen Feng, Shuguang Zhai, Jun Yu, Weijie Zhu, Yuxia Kong, et al.

Environmental Science and Pollution Research

ISSN 0944-1344
Volume 27
Number 7

Environ Sci Pollut Res (2020)
27:7005-7014
DOI 10.1007/s11356-019-06427-w

Springer

Environmental Science and Pollution Research (2020) 27:7005–7014
https://doi.org/10.1007/s11356-019-06427-w

RESEARCH ARTICLE

Chemical content and source apportionment of 36 heavy metal analysis and health risk assessment in aerosol of Beijing

Limeng Cui[1,3] · Zhuona Wu[2] · Peng Han[2] · Yasuyuki Taira[3] · Huan Wang[1] · Qinghua Meng[1] · Zechen Feng[1] · Shuguang Zhai[1] · Jun Yu[1] · Weijie Zhu[1] · Yuxia Kong[1] · Hongfang Wang[1] · Hong Zhang[1] · Bin Bai[1] · Yun Lou[1] · Yongzhong Ma[1]

Received: 15 February 2019 / Accepted: 4 September 2019 / Published online: 27 December 2019

Abstract

The concentration levels of 36 airborne heavy metals and atmospheric radioactivity in total suspended particulate (TSP) samples were measured to investigate the chemical characteristics, potential sources of aerosols, and health risk in Beijing, China, from September 2016 to September 2017. The TSP concentrations varied from 6.93 to 469.18 μg/m^3, with a median of 133.97 μg/m^3. The order for the mean concentrations of heavy metals, known as hazardous air pollutants (HAPs), was as follows: Mn > Pb > As > Cr > Ni > Se > Cd > Co > Sb > Hg > Be; Non-Designated HAPs Metals: Ca > Fe > Mg > Al > K > Na > Zn > P > Ba > Ti > Cu > Sr > B > Sn > I > V > Rb > Ce > Mo > Cs > Th > Ag > U > Pt. The median concentration of As was higher than China air quality standard (6 ng/m^3). The gross α and β concentration levels in aerosols were (1.84 ± 1.59) mBg/m^3 and (1.15 ± 0.85) mBg/m^3, respectively. The enrichment factor values of Cu, Ba, B, Ce, Tl, Cs, Pb, As, Cd, Sb, Hg, Fe, Zn, Sn, I, Mo, and Ag were higher than 10, which indicated enriched results from anthropogenic sources. Pb, As, and Cd are considered to originate from multiple sources; fireworks released Ba during China spring festival; Fe, Ce, and Cs may come from stable emissions such as industrial gases. The health risks from anthropogenic metals via inhalation, ingestion, and dermal pathway were estimated on the basis of

Responsible editor: Gerhard Lammel

✉ Yongzhong Ma
myz0905@126.com

Limeng Cui
cuilimeng1103@sina.com

Zhuona Wu
wznbaobao@163.com

Peng Han
18612835949@163.com

Yasuyuki Taira
y-taira@nagasaki-u.ac.jp

Huan Wang
cdcwanghuan@aliyun.com

Qinghua Meng
mengqinghua6@sina.com

Zechen Feng
fzcjlu@163.com

Shuguang Zhai
Zhaishuguang@163.com

Jun Yu
yujun-fs@163.com

Weijie Zhu
215822525@qq.com

Yuxia Kong
174225964@qq.com

Hongfang Wang
wanghf@jlu.edu.cn

Hong Zhang
zhanghong423@sohu.com

Bin Bai
541009783@qq.com

Yun Lou
louyun118@263.net

1 Department of Radiation protection, Beijing Municipal Center for Disease Prevention and Control, Beijing Research Center for Preventive Medicine, Beijing 100013, China

2 Institute of Radiation Medicine, Academy of Military Medical Science, Beijing 100850, China

3 Atomic Bomb Disease Institute, Nagasaki University, Nagasaki 8528523, Japan

health quotient as well as the results indicated that children faced the higher risk than adults during the research period. For adults, the health risk posed by heavy metals in atmospheric particles was below the acceptable level.

Keywords Heavy metals, · Atmospheric radioactivity, · Enrichment factor, · Hazard quotient

Introduction

Air pollution is a global threat with negative effects on public health and ecosystems (European Environment Agency 2018). Severe air pollution not only increases the risk of cancer, but also may lead to cardiovascular or chronic obstructive pulmonary disease, allergies, and Alzheimer's disease (WHO 2013a; Sun et al. 2014b; Morishita et al. 2015; Zhang et al. 2016; Kilian and Kitazawa 2018). Previous studies suggested the cardiovascular effects of ambient air particulate matter (PM) are greatly influenced by their metal contents (nickel) (Zanobetti et al. 2009; Mostofsky et al. 2012).

Some heavy metals in atmospheric particles can severely affect human health (WHO 2000, 2013b; U.S. EPA 2016, 2019a). For instance, arsenic (As) can increase incidence of lung cancer (WHO 2000); lead (Pb) can adversely affect the nervous system, kidney function, immune system, reproductive and developmental systems, and cardiovascular system (UNEP, 2010; U.S. EPA 2007); mercury (Hg) intake in China leads to fetus intelligence quotient decrements and fatal heart attacks (Chen et al. 2019). Although some metallic elements, such as iron (Fe), are indispensable to the human body, excessive amounts of these metals still present health risks (Geiger and Cooper 2010).

Atmospheric radioactivity originated from the naturally occurring radioisotopes, such as Thorium-232 (^{232}Th) and Uranium-238 (^{238}U) series and their decay products, nuclear accident, and nuclear testing (UNSCEAR 2000; Tzortzis and Tsertos 2004). The inhalation of radioactive atmospheric particles is one of the natural radiation sources for human beings (UNSCEAR 2000). Therefore, gross alpha (α) and beta (β) are generally measured for screening unusual radioactivity in the atmosphere (Dueñas et al. 1999).

Beijing, as the capital of China, has a high population density and the largest vehicle ownership rates in China (about 6 million and 80 thousand vehicles in 2018) (The People's Government of Beijing Municipality 2018; Beijing Traffic Management Bureau 2019). From 2013 to 2017, the fine particle pollution decreased from 89.5 to 58 μg/m^3 in Beijing but still exceeds the national standard by 66% (Fig. 1) (UN environment 2019). Furthermore, the provinces around Beijing, such as Tianjin and Hebei, have a relatively large industrial emission (Li et al. 2018a; Yang et al. 2019). Previous studies in Beijing reported high health risks and related health impact caused by heavy metals in air particulate matter (Langrish et al. 2009; Rich et al. 2012; Du et al. 2013; Shao et al. 2017; Li et al. 2018b; Yue et al. 2019). Therefore, the study of heavy metals in atmospheric particles is significant to the haze pollution control and human health protection.

Thus, in this study, we analyzed the levels of metals and gross radioactivity of total suspended particulate (airborne particles with diameters less than 100 μm, TSP) samples in Beijing, China. Moreover, possible risk sources were identified and analyzed. Finally, the results of element concentrations were also used to develop a quantitative estimate of the health quotients (HQs).

Methodology

Air sampling collection and metal measurement

The measurements occurred on the rooftop of an office building (20 m above ground) at Hepingli Zhongjie, Dongcheng District, Beijing (116.2° E, 39.6° N) (Fig. 1). The site is located in a mixed-use neighborhood including schools, residences, and parks. The site is also in close proximity to two major streets, i.e., the second ring road around Beijing (approximately 1 km south) and the third ring road (approximately 2 km north).

Seventy-five TSP samples were collected by a high-volume air sampler (Senya, Sweden, Snow White, 900 m^3/h) from September 2016 to September 2017. The collecting time for each sample was 24 h. To analyze the seasonal variation, the average of each season (spring: n = 15, 2017/3/2–2017/5/18; summer: n = 11, 2017/6/3–2017/8/25; autumn: n = 26,2016/9/28–2016/11/29, 2017/9/3–2017/9/22; winter: n = 21, 2016/12/2–2017/2/23) was used to draw a percentage stacked column chart (Fig. 1). The air volume that passed through the sampler (10-μm pore size) was 13709~26090 m^3/day.

In this work, 36 metal elements were analyzed: manganese (Mn), arsenic (As), cadmium (Cd), nickel (Ni), chromium (Cr), lead (Pb), selenium (Se), antimony (Sb), mercury (Hg), beryllium (Be), cobalt (Co), iron (Fe), calcium (Ca), magnesium (Mg), aluminum (Al), potassium (K), sodium (Na), zinc (Zn), phosphorus (P), barium (Ba), titanium (Ti), copper (Cu), strontium (Sr), boron (B), tin (Sn), iodine (I), vanadium (V), rubidium (Rb), cerium (Ce), molybdenum (Mo), thallium (Tl), cesium (Cs), thorium (Th), argentum (Ag), uranium (U), platinum (Pt). The results of heavy metals were divided to hazardous air pollutant (HAP) group and non-designated HAP group on the basis of *the Initial List of Hazardous Air Pollutants with Modifications* (U.S.EPA 2010; U.S. EPA 2016). Mn, Pb, As, Cr, Ni, Se, Cd, Co, Sb, Hg, and Be and

Fig. 1 The map of Beijing and the surroundings with sampling point (red triangle). L. M. C. created the map using the software Green Map® (Tokyo Shoseki Co., Ltd., Tokyo, Japan)

their compounds are included in the list. Although the other 25 metals have not been designated as hazard air pollution yet, excessive amounts of these metals still present health risks.

The net weight of TSP was obtained by weighing the filter membrane after sampling and subtracting the membrane weight before sampling. The TSP concentrations were obtained by dividing the net sampling weight by the sampling flow rates.

Air pollution data (PM2.5, PM10) were obtained from the website of Beijing municipal ecological environmental bureau (Beijing Municipal Ecological Environmental Bureau 2019). The temperature and relative humidity during sampling were derived from the website of Wunderground website (www.wunderground.com).

A low background alpha, beta measurement apparatus is a lower cost device that is widely used in environmental sample monitoring. By using standard sampling methods and standard ways of processing and storing, we choose Americium-241 (Am-241) and Potassium-40 (K-40) as standard materials to conduct the experiment by employing qualified drugs and reagents. To ensure the veracity of the method, all devices and instruments that are involved are calibrated by the National Institute of Metrology and are still in the validity period.

The elemental analysis was performed using 7700x Agilent inductively coupled plasma mass spectrometry (ICP-MS, American) and Mass Hunter Workstation Software (Version: A.01.02; Agilent Technologies). Calibrants were prepared from multi-element standard solution (Lot: S130823001,Canada, Plasma CAL). The samples (including blank membrane samples) were digested by adding 10 mL concentrated nitric acid and digested according to the microwave procedure. After the acid wiped out, volume was 50 mL with pure water for determination. Quantitative analysis of the elemental concentrations in unknown samples was measured by an internal standard method.

Enrichment factor and health risk assessment

To determine whether the presence of a certain element was due to natural or anthropogenic sources, the enrichment factor (Ef) value was eliminated to indicate the source identification of heavy metal abundances in the atmosphere. Al is used as a reference element since it is ubiquitous in the environment and has no significant anthropogenic sources. The Ef of heavy metals can be calculated using the following equation (Taylor S.R 1964; Hsu et al. 2010):

$$\mathrm{Ef} = \frac{(\mathrm{C}/\mathrm{Al})_{\mathrm{aerosol}}}{(\mathrm{C}/\mathrm{Al})_{\mathrm{Crust}}} \quad (1)$$

where $(C/Al)_{aerosol}$ is the concentration ratio of given heavy metals C to Al in ambient samples, and $(C/Al)_{crust}$ is the same ratio of the heavy metal C to Al in the average samples. The background concentrations of heavy metals in the background are selected in China (Li Tong 1997).

Previous studies show that Ef values lower than 10 suggest a greater possibility of pollution from natural crustal elements, while values between 10 and 100 should be considered to indicate that elements are from human activities and mixed sources (from both natural and anthropogenic sources); high Ef values (> 100) are considered to be the result of anthropogenic sources or exceptional geological events (Betha et al. 2014; Lyu et al. 2017). However, studies support different standards with Ef values between 2 and 10 being suggestive of moderate mixed sources (Li Tong 1997; Lin et al. 2016).

Human health can be significantly influenced by heavy metals in the atmosphere via ingestion, dermal contact, and inhalation (WHO 2000). The exposure parameters for exposure assessment models are referenced from the U.S. EPA, environmental site assessment guidelines, and other relative studies (U.S. EPA 2009; Du et al. 2013; Sun et al. 2014a; Wei et al. 2015; Zheng et al. 2015; Zhang et al. 2016; Megido et al. 2017; Kicinska and Bozecki 2018).

The average daily dose (mg/kg day^{-1}, ADD) was estimated for each element using the following expressions:

$$ADD_{ing} = \frac{C \times IR_{ing}}{BW} \times \frac{EF \times ED}{AT} \times CF \quad (2)$$

$$ADD_{derm} = \frac{C \times SA \times AF \times ABS}{BW} \times \frac{EF \times ED}{AT} \times CF \quad (3)$$

$$ADD_{inh} = C \times IR_{inh} \times \frac{EF \times ED}{BW \times AT_n} \times \mathbf{CF} \quad (4)$$

where C (ng/m^3) is the metal concentration in TSP; IR is the ingestion rate (100 mg/day for adults and 200 mg/day for children), and inhalation rate (20 m^3/day for adults and 5 m^3/day for children) (Vik et al. 1999; Du et al. 2013); BW is the average body weight of Beijing citizen (66.1 kg for adults and 22.7 kg for children) (He et al. 2016; Meng Jie et al. 2017); EF is the exposure frequency (350 days/year) (U.S. EPA 2014); ED is the exposure duration (24 years for adults and 6 years for children) (U.S. EPA 2014); AT is the average time (365 days × ED); CF is the conversion factor (1 × 10^{-6} kg/mg) (U.S. EPA 1989); SA is the surface exposure area of Chinese in summer (4020 cm^2 for adults and 2160 cm^2 for children) (Zong et al. 2009); AF is the adherence factor (0.07 mg/cm^2/day for adults and 0.02 mg/cm^2/day for children) (U.S. EPA 2004); ABS is the dermal absorption factors (0.03 (As), 0.001 (Cd), 0.01 (others)) (Hu et al. 2012; Megido et al. 2017; U.S. EPA 2019b); AT_n = ED × 365 days× 24 h/day.

The assessment of potential health risks uses the following equation (U.S. EPA 2009):

$$HQ_{sum} = \sum_{i=1}^{3} HQ_i = \sum_{i=1}^{3} \frac{ADD_i}{RfD_i} \quad (5)$$

where RfD refers to the reference dose for the pathways which are listed in Table 1. HQ ≤ 1 indicates no adverse health effects, and HQ ≥ 1 shows a probability of adverse health effects (U.S. EPA 2001).

In this study, the hazard quotient was calculated only for heavy metals with Ef values greater than 10, which are from anthropogenic sources. Although the Fe, Mg, Ca, K, and Na are essential human nutrients and are toxic only at very high doses, we calculate the HQ for Fe due to the higher Ef value (U.S. EPA 1989).

Statistical analysis

Mean, standard deviation, and minimum and maximum values of air pollutant concentrations were calculated for descriptive statistics. Spearman's non-parametric rank order correlation coefficient was used to describe the correlation among TSP, temperature, humility, seasonal variations, gross α and β, and heavy metals. The regression lines were used to calculate the percentage of PM_{10} and $PM_{2.5}$ in TSP. The criterion for statistical significance was $p < 0.05$. Statistical analysis was performed using a SPSS 25 (IBM Corp., Armonk, NY, USA).

Results and discussion

The concentration of heavy metals and gross radioactivity

The TSP, gross radioactivity, and concentration of metal elements in the aerosol samples collected in Beijing from September 2016 to September 2017 are reported in Table 2.

During the sampling period, the TSP concentrations varied from 6.93 to 469.18 μg/m^3, with a median of 133.97 μg/m^3. The $PM_{2.5}$ and PM_{10} concentrations obtained from the website of Beijing municipal ecological environmental bureau ranged from 6 to 430 μg/m^3 (6–510 g/m^3), with a median of 52 μg/m^3 (79 μg/m^3) (Beijing Municipal Ecological Environmental Bureau 2019). The $PM_{2.5}$ and PM_{10} concentrations were compared with the TSP concentrations to determine the proportion in TSP from the regression lines. The results show that, in this study, the $PM_{2.5}$ and PM_{10} took about 48% and 68% of TSP samples, respectively.

The average concentration of radioactivity in this research (gross α, 1.84 mBg/m^3; gross β, 1.15 mBg/m^3) was still clearly higher in the majority. Previous studies conducted in Qinshan nuclear power plant, Spain, and New Mexico have reported that the average of gross α and gross β ranged from 0.069 to 0.357 mBg/m^3 and 0.45 to 1.0 mBg/m^3, respectively (García-Talavera et al. 2001; Hernández et al. 2005; Bin et al. 2007; Huang et al. 2009; Thakur and Mulholland 2011). It should be noticed the average concentrations of natural radon in modern buildings is about 50 Bq/m^3 which is extremely higher than the gross α and β concentration in outdoor air (Malinovsky et al. 2018). The health risks caused by the inhalation of radioactive particles in the air are mainly considered indoor source rather than outdoor.

For Pb, Cd, and Hg, although the median values did not exceed limits of China (Pb 0.5 μg/m^3, Cd 5 ng/m^3, Hg 50 ng/m^3) (Ministry of Environmental Protection (China) 2012), the mean concentration of Pb exceeded the ambient air quality standard of the USA (0.15 μg/m^3) (U.S. EPA 2019). Compared with the WHO proposed limit values (0.5 μg/m^3 for Pb, 1 μg/m^3 for Mn, 4–13 ng/m^3 for As, 5 ng/m^3 for Cd, 1 μg/m^3 for Hg, and 20 ng/m^3 for Ni) and China air quality standard (6 ng/m^3 for As), the median concentrations of Pb, Mn, Cd, Hg, and Ni were lower than the limit except As (Van Leeuwen 2002; Ministry of Environmental Protection (China) 2012; WHO 2013a, 2017; Padoan et al. 2016). The average concentrations of As and Pb were higher than other studies

Table 1 Reference factors for assessing hazard quotient (U.S. EPA 2009, 2011, 2019b; Du et al. 2013; Sun et al. 2014a; Wei et al. 2015; Zheng et al. 2015; Zhang et al. 2016; Megido et al. 2017; Liu et al. 2018; Kicinska and Bozecki 2018)

Element	RfD_{der}—dermal reference	RfD_o—oral reference	RfC_i—inhalation reference
Pb	5.2E−04	3.5E−03	
As		3.00E−04	1.50E−05
Cd	1.00E−05	1.00E−05	1.00E−03
Sb		4.00E−04	3.0E−04
Hg		1.60E−04	3.0E−04
Fe		7.00E−01	
Zn	6E−02	3.00E−01	
Ba		2.00E−01	5.0E−04
Cu	1.2E−02	4.00E−02	
B		2.00E−01	2.0E−02
Sn		6.00E−01	
I		5.04E−03	
Mo		5.00E−03	4.0E−04
Tl			1.0E−04
Ag		5.00E−03	

conducted in Beijing during 2016 and 2017 which was reverse for Cr and Fe (Liu et al. 2018; Men et al. 2018; Jin et al. 2019). Although those researches were conducted in Beijing during a similar time period, the results showed difference which the heavy metals were considered to regional differences of pollution sources.

Seasonal distribution pattern and source analysis

The percentage of gross α and β, Pb, As, Se, Cd, Sb, Hg, K, Na, Ba, Cu, Sr, B, I, Mo, and Tl in winter exceed 50% of the whole year (Fig. 2). Gross α, gross β, Pb, As, Cr, Se, Cd, Sb, Hg, K, Na, Zn, Ba, Cu, Sr, B, Sn, I, Mo, Tl, Ag, and Pt are significantly correlated with seasonal variations ($p < 0.05$).

There were negative associations between temperature and concentration of heavy metals except Sn as well as between temperature and gross radioactivity ($p < 0.05$). The concentrations of Pb, As, Se, Cd, Sb, Hg, Zn, Sn, Mo, Tl, and Ag were correlated with humidity ($p < 0.05$). The statistical results of the Spearman correlation between gross radioactivity and 36 metal elements showed positively correlations ($p < 0.05$).

Figure 3 shows the enrichment factor (Ef) of each element calculated to evaluate the anthropogenic influence. On the basis of the mean concentration of elements, the Ef values of Cu, Ba, B, Ce, Tl, and Cs were between 10 and 100, which indicated anthropogenic sources instead of crustal sources. The Ef values of Pb, As, Cd, Sb, Hg, Fe, Zn, Sn, I, Mo, and Ag were higher than 100, which indicated highly enriched results from anthropogenic sources.

In China, metal elements in coal include I, Be, Cr, Co, Ni, Cu, As, Se, Sr, Mo, Cd, Sb, Cs, Hg, Pb, Th, U, and Ba (Dai et al. 2012; Gao et al. 2018). Some research suggested the use of Cr, Ni, Hg, and As as markers of coal combustion in China (Tian et al. 2010; Kittner et al. 2018), and coal combustion emissions are considered the main source of pollution in Beijing (Cai et al. 2017). Cd, Cu, Pb, Zn, As, and Ni were suggested to be associated with diesel and gasoline exhaust fumes from local traffic and other anthropogenic emissions (Valavanidis et al. 2006; Men et al. 2018). A study suggests that anthropogenic sources such as brake wear, tire dust, road abrasion, and fossil fuel combustion spread Cu, Sb, Pb, and Zn (Dehghani et al. 2017). Tl is considered a characteristic element of heavy industries (Lin et al. 2016). Cu, Sn, and Ag were usually used as solder alloys (Miller et al. 1994).

In winter, 21 (As, Cd, Fe, Pb, Zn, Hg, Sb, Cu, Mo, Ag, Sn, I, Cs, Ce, Tl, B, Ba, Pt, P, and Ca) of the 36 trace metals are predominantly of anthropogenic origin, with concentrations dependent on the level of anthropogenic activities. Ba, Pt, P, and Ca (Ef: 24.5, 10.5, 10.5, 10.9, respectively) showed anthropogenic origin in winter only. Pt is the major constituent of automotive catalysts (Nischkauer et al. 2017). If this is the reason for the increase of Ef value, it should be reflected in four seasons; therefore, these three elements are considered to be more easily affected by air diffusion. It should be noted that the highest concentration of Ba (the Ef values are lower than 10 in other seasons) was in February 1, 2017, which was the day of the Chinese Spring Festival when people used fireworks containing Ba to celebrate. The Ef values of I, Hg, Mo, Sb, and Zn are higher than 10, have an obvious correlation with seasons, and belong to coal metal elements (Tian et al. 2010; Dai et al. 2012; Gao et al. 2018; Kittner et al. 2018). Therefore, according to these elements, coal combustion emissions are considered to be the main source.

Most elements with an Ef value greater than 10 are significantly correlated with seasonal variations exempting Fe, Ce, and Cs. This suggests these three elements may come from stable emissions such as industrial gases. This is consistent with the findings of Yu-Chi Lin et al., which suggested the source of Fe in Beijing was mainly from iron and steel manufacturing (Lin et al. 2016). Ce is widely used as an automobile exhaust purification catalyst (Jung et al. 2005). At

Table 2 Mean, minimum, and maximum concentrations of each element determined in PM_{10} samples in Beijing from September 2016 to September 2017. All values, except for TSP, and gross α and β, are expressed in ng/m^3. TSP is expressed in μg/m^3. Gross α and β are expressed in mBg/m^3

		Median	Min	Max	Mean	SD
TSP		1.34E+02	6.93E+00	4.69E+02	1.52E+02	1.04E+02
Gross α		1.62E+00	1.45E−02	9.41E+00	1.84E+00	1.59E+00
Gross β		9.97E−01	1.33E−02	3.91E+00	1.15E+00	8.54E−01
Hazardous air pollutants (HAPs)	Mn	1.64E+02	2.51E+01	2.17E+03	2.12E+02	2.6E+02
	Pb	9.79E+01	2.87E+00	3.22E+03	1.93E+02	3.9E+02
	As	1.05E+01	4.55E−01	3.88E+02	2.70E+01	5.1E+01
	Cr	1.65E+01	1.94E+00	2.50E+02	2.22E+01	3.0E+01
	Ni	9.12E+00	1.08E+00	1.40E+02	1.20E+01	1.7E+01
	Se	5.00E+00	1.12E−01	1.71E+02	1.00E+01	2.1E+01
	Cd	2.11E+00	4.73E−02	8.79E+01	4.70E+00	1.1E+01
	Co	2.46E+00	2.72E−01	4.08E+01	3.50E+00	4.8E+00
	Sb	9.95E−01	9.06E−02	9.04E+01	3.30E+00	1.1E+01
	Hg	2.32E−01	7.51E−03	1.11E+01	5.00E−01	1.3E+00
	Be	1.60E−01	1.95E−02	2.83E+00	2.00E−01	3.0E−01
Non-designated HAPs Metals	Ca	1.22E+04	1.81E+03	1.23E+05	1.47E+04	1.5E+04
	Fe	4.77E+03	6.25E+02	5.64E+04	6.17E+03	7.0E+03
	Mg	2.66E+03	4.01E+02	2.72E+04	3.41E+03	3.4E+03
	Al	2.06E+03	3.12E+02	2.42E+04	2.97E+03	3.2E+03
	K	1.65E+03	1.25E+02	3.29E+04	2.77E+03	4.4E+03
	Na	1.16E+03	6.19E+01	5.42E+04	2.52E+03	6.4E+03
	Zn	3.04E+02	1.32E+01	6.80E+03	4.76E+02	8.1E+02
	P	1.88E+02	2.32E+01	3.16E+03	2.53E+02	3.7E+02
	Ba	1.18E+02	1.43E+01	2.23E+03	2.06E+02	3.5E+02
	Ti	9.54E+01	1.34E+01	1.29E+03	1.24E+02	1.6E+02
	Cu	6.79E+01	7.62E+00	1.56E+03	1.15E+02	1.9E+02
	Sr	4.04E+01	4.48E+00	7.27E+02	6.47E+01	1.0E+02
	B	1.17E+01	6.30E−01	7.18E+02	3.05E+01	8.4E+01
	Sn	1.04E+01	1.69E+00	2.07E+02	1.68E+01	2.5E+01
	I	5.72E+00	2.46E−01	1.97E+02	1.15E+01	2.4E+01
	V	9.26E+00	1.02E+00	8.44E+01	1.11E+01	1.1E+01
	Rb	6.70E+00	6.68E−01	9.41E+01	9.20E+00	1.2E+01
	Ce	5.57E+00	7.86E−01	1.12E+02	8.50E+00	1.3E+01
	Mo	3.32E+00	2.70E−01	6.73E+01	5.20E+00	8.3E+00
	Tl	1.04E+00	2.98E−02	3.88E+01	2.10E+00	4.7E+00
	Cs	8.44E−01	8.57E−02	1.19E+01	1.20E+00	1.6E+00
	Th	7.89E−01	1.04E−01	1.04E+01	1.11E+00	1.32E+00
	Ag	3.44E−01	1.13E−02	7.67E+00	6.00E−01	1.0E+00
	U	2.46E−01	2.73E−02	4.07E+00	3.44E−01	4.95E−01
	Pt	1.85E−03	9.00E−06	9.77E−03	2.20E−03	1.9E−03

present, the largest use of non-radioactive Cs is as a specialty high-density component in drilling mud used for petroleum exploration (Butterman et al. 2004). The industrial enterprises were the main reason for concentrations of Fe, Ce, and Cs in Beijing.

The higher contents of elements in aerosols are considered to originate from multiple sources. Firstly, in Beijing, the sources of Cd may come from burning fossil fuels, municipal waste material incineration, tire wear friction, and cigarette smoking (Geiger and Cooper 2010; Men et al. 2018). Secondly, Pb and As were anthropogenic in origin and changed with seasons. Potential sources include coal, motor vehicles, and industrial operations (Valavanidis et al. 2006; Dehghani et al. 2017). Furthermore, the industrial As include wood preserving industry paints, dyes, metals, drugs, soaps, and semi-conductors (Geiger and Cooper 2010). Although leaded gasoline has been banned in some megacities in China, Pei-Hsuan Yao et al. suggests that local unleaded fuel combustion still was a Pb

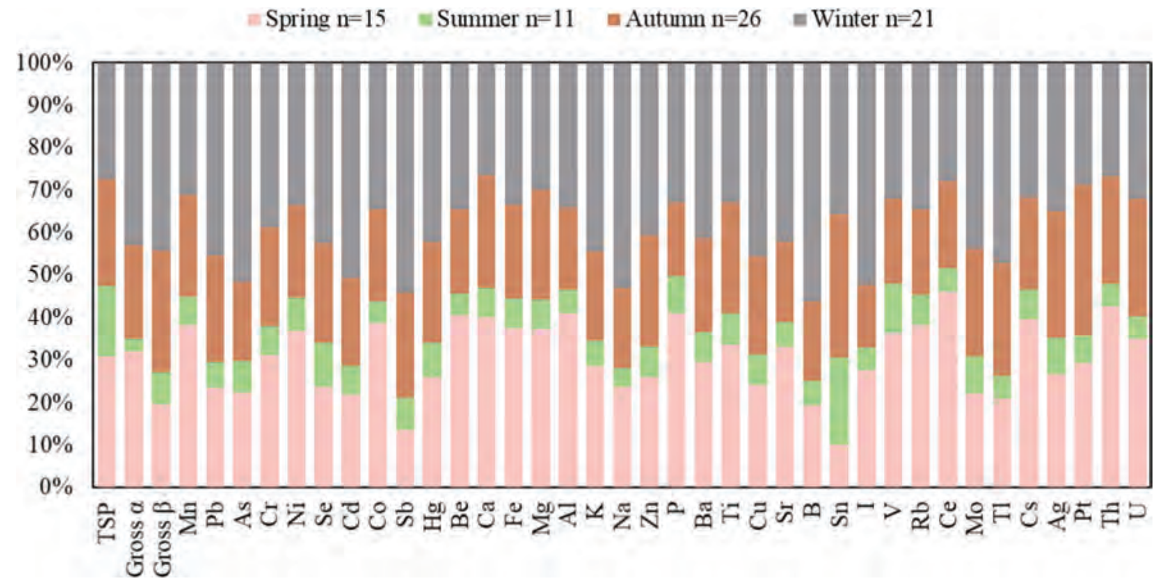

Fig. 2 The distribution of average concentration of gross radioactivity and metal elements in different seasons

contributor to the metropolitan air (Yao et al. 2015). Ore and metal processing as well as piston-engine aircraft operations using leaded aviation fuel also are considered lead sources (U.S. EPA). The seasonal differences of Pb in this study indicates that the main source of Pb in Beijing may not only come from stable release but the atmospheric dispersion conditions and coal combustion emissions in winter (Geiger and Cooper 2010).

Hazard quotient

Table 3 showed the hazard quotients of anthropogenic source metals (Pb, As, Cd, Sb, Hg, Fe, Zn, Ba, Cu, B, Sn, I, Mo, Tl, and Ag) via ingestion, dermal contact, and inhalation for children and adults. The mean HQ of As was the highest among both children and adults. The order of HQ in children and adult groups is As, Pb, Ba, Fe, Sb, Cu, Hg, I, Zn, Mo, Cd, Tl, B, Ag, and Sn and As, Ba, Pb, Sb, Fe, Cd, Tl, Cu, Mo, Hg, I, Zn, B, Ag, and Sn.

For adults, the average values of HQ for none of the metals exceeded 1, indicating the health risk posed by heavy metals in atmospheric particles was acceptable during the research period. However, the integrated risks of these metals were higher to children (1.98), while the risks through ingestion were 1.48. The contribution of risks through ingestion to HQ were 74.7% and 25.6% for children and adults, respectively. The higher ingestion rate of children was supposed to be the main reason and similar results were also obtained by other scholars (Lyu et al. 2017; Men et al. 2018). The results confirmed that from September 2016 to September 2017, the air pollution problems in Beijing was still serious for children.

Uncertainty and limitations

The risk estimation in this study has certain limitations and may have a degree of uncertainty, because only one sample site in the city center was used and all applied parameters are assumed to be ideal. It will more reasonable if sampling sites were separated in different functional areas such as industrial

Fig. 3 Average enrichment factor values for HAP metals (red points) and non-designated HAP metals (blue points) collected in Beijing from September 2016 to September 2017

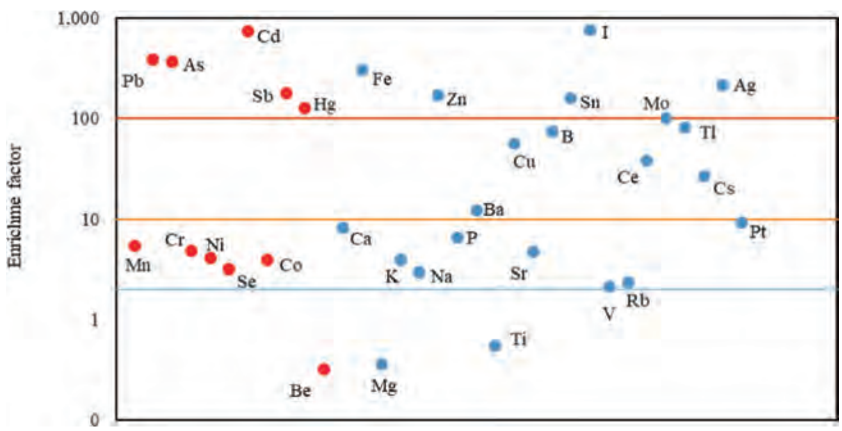

Table 3 The average hazard quotient (HQ) from heavy metals in TSP via inhalation (inh), ingestion (ing), and dermal contact (derm)

		HQ_{inh}		HQ_{ing}		HQ_{derm}		HQ_{sum}	
		Adults	Children	Adults	Children	Adults	Children	Adults	Children
	Pb	1.6E−02	1.2E−02	8.0E−02	4.7E−01	1.5E−02	6.7E−03	1.1E−01	4.8E−01
Hazardous Air Pollutants (HAP)	As	5.2E−01	3.8E−01	1.3E−01	7.6E−01	6.3E−03	2.8E−03	6.6E−01	*1.1E+00*
	Cd	1.4E−06	1.0E−06	6.8E−04	4.0E−03	7.7E−03	3.4E−03	8.4E−03	7.4E−03
	Sb	3.2E−03	2.3E−03	1.2E−02	6.9E−02			1.5E−02	7.2E−02
	Hg	4.5E−04	3.3E−04	4.2E−03	2.5E−02			4.7E−03	2.5E−02
Non−designated HAP metals	Fe			1.3E−02	7.4E−02			1.3E−02	7.4E−02
	Zn	4.7E−04	3.4E−04	2.3E−03	1.4E−02	3.3E−04	1.5E−04	3.1E−03	1.4E−02
	Ba	1.2E−01	8.7E−02	1.5E−03	8.7E−03			1.2E−01	9.6E−02
	Cu	8.3E−04	6.1E−04	4.2E−03	2.4E−02	3.9E−04	1.7E−04	5.4E−03	2.5E−02
	B	4.4E−04	3.2E−04	2.2E−04	1.3E−03			6.6E−04	1.6E−03
	Sn			4.1E−05	2.4E−04			4.1E−05	2.4E−04
	I			3.3E−03	1.9E−02			3.3E−03	1.9E−02
	Mo	3.8E−03	2.8E−03	1.5E−03	8.9E−03			5.3E−03	1.2E−02
	Tl	6.2E−03	4.5E−03					6.2E−03	4.5E−03
	Ag			1.8E−04	1.0E−03			1.8E−04	1.0E−03
SUM		6.73E−01	4.90E−01	2.54E−01	*1.48E+00*	2.98E−02	1.33E−02	9.56E−01	*1.98E+00*

The italicized values means a probability of adverse health effects

zone and a residential zone. In addition, the differences (TSP vs $PM_{2.5}$) exist in particle bound elements because of the pore size of filter (10 μm) in this study. Future studies need to consider the health risks posed by airborne heavy metals in $PM_{2.5}$. Because the measurement station is 20 m above the ground, the risk estimates may be biased compared to the risks of real public outdoor activities.

Despite these shortcomings, the risk model and conclusions of this study provide a basis for assessing and future monitoring of human health risk associated with metal exposure in Beijing, China.

Conclusions

In this study, 36 elements were measured, including some previously neglected elements, such as Ce, Cs, I, and Ag, to provide more comprehensive data to examine air pollution sources. In addition, the health risks caused by the inhalation are mainly considered indoor source rather than outdoor. Furthermore, on the basis of the enrichment factors, we confirmed that Pb, As, Cd, Sb, Hg, Fe, Zn, Cu, Ba, B, Sn, I, Mo, Ce, Tl, Cs, and Ag were the anthropogenic heavy metal aerosols. The health risks posed by heavy metals in atmospheric particles were below the acceptable level for adults as well as the children faced higher health risk than adults. Further research is needed because there is concern about health effects due to air pollution.

Author contributions Conceptualization, funding acquisition, and supervision, Y. Z. M; formal analysis, investigation, methodology, and writing, L. M. C.; methodology and resources, Z. N. W. and P. H.; review and editing, Y. T.; resources, Y. Z. M., Y. L., B. B., H. Z., Y. X. K., W. J. Z., J. Y., S. G. Z., Q. H. M., H. F. W., and H. W.; all authors helped approve the final manuscript with discussions.

Funding information This work was supported by the Special Fund for Scientific Research Projects of Beijing Municipal Center for Disease Prevention and Control/Beijing Research Center for Preventive Medicine (no. 2016-BJYJ-18) and Japan China Sasakawa Medical Fellowship.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

References

Beijing Municipal Ecological Environmental Bureau (2019) Real-time air quality (in Chinese). In: http//zx.bjmemc.com.cn/?timestamp = 1565074336255 (Accessed August 24 2019)

Beijing Traffic Management Bureau (2019) Traffic management since 2000 (in Chinese). In: http//bjjtgl.gov.cn/jgj/ywsj/index.html (Accessed August 3, 2019)

Betha R, Behera SN, Balasubramanian R (2014) 2013 Southeast Asian smoke haze: fractionation of particulate-bound elements and associated health risk. Environ Sci Technol 48:4327–4335. https://doi.org/10.1021/es405533d

Bin C, Qianyuan C, Xiaofei WU, Hongfeng W (2007) Activity level of gross α and gross β in airborne aerosol samples around the Qinshan NPP. Nucl Sci Tech 18:176–180

Butterman BWC, Brooks WE, Reese RG (2004) Cesium

Cai J, Wang J, Zhang Y et al (2017) Source apportionment of Pb-containing particles in Beijing during January 2013. Environ Pollut 226:30–40. https://doi.org/10.1016/j.envpol.2017.04.004

Chen L, Liang S, Liu M et al (2019) Trans-provincial health impacts of atmospheric mercury emissions in China. Nat Commun 10:1–12. https://doi.org/10.1038/s41467-019-09080-6

Dai S, Ren D, Chou CL et al (2012) Geochemistry of trace elements in Chinese coals: a review of abundances, genetic types, impacts on human health, and industrial utilization. Int J Coal Geol 94:3–21. https://doi.org/10.1016/j.coal.2011.02.003

Dehghani S, Moore F, Keshavarzi B, Hale BA (2017) Health risk implications of potentially toxic metals in street dust and surface soil of Tehran, Iran. Ecotoxicol Environ Saf 136:92–103. https://doi.org/10.1016/j.ecoenv.2016.10.037

Du Y, Gao B, Zhou H et al (2013) Health risk assessment of heavy metals in road dusts in urban parks of Beijing, China. Procedia Environ Sci 18:299–309. https://doi.org/10.1016/j.proenv.2013.04.039

Dueñas C, Fernández MC, Liger E, Carretero J (1999) Gross alpha, gross beta activities and 7Be concentrations in surface air: analysis of their variations and prediction model. Atmos Environ. https://doi.org/10.1016/S1352-2310(99)00172-7

European Environment Agency (2018) Air quality in Europe

Gao Y, Yang C, Ma J, Yin M (2018) Characteristics of the trace elements and arsenic, iodine and bromine species in snow in east-central China. Atmos Environ 174:43–53. https://doi.org/10.1016/j.atmosenv.2017.11.015

García-Talavera M, Quintana B, García-Díez E, Fernández F (2001) Studies on radioactivity in aerosols as a function of meteorological variables in Salamanca (Spain). Atmos Environ 35:221–229. https://doi.org/10.1016/S1352-2310(00)00234-X

Geiger A, Cooper J (2010) Overview of airborne metals regulations, exposure limits, health effects, and contemporary research. 1–50. https://doi.org/10.1212/01.CON.0000480843.89012.5b

He Y, Zeng Q, Zhao X (2016) Associations of body mass index and age with blood pressure among chi- nese adults(Chinese). Chin J Public Health 32:126–129

Hernández F, Hernández-Armas J, Catalán A et al (2005) Gross alpha, gross beta activities and gamma emitting radionuclides composition of airborne particulate samples in an oceanic island. Atmos Environ 39:4057–4066. https://doi.org/10.1016/j.atmosenv.2005.03.035

Hsu SC, Liu SC, Tsai F et al (2010) High wintertime particulate matter pollution over an offshore island (Kinmen) off southeastern China: an overview. J Geophys Res Atmos 115:1–17. https://doi.org/10.1029/2009JD013641

Hu X, Zhang Y, Ding Z et al (2012) Bioaccessibility and health risk of arsenic and heavy metals (Cd, Co, Cr, Cu, Ni, Pb, Zn and Mn) in TSP and PM2.5 in Nanjing, China. Atmos Environ 57:146–152. https://doi.org/10.1016/j.atmosenv.2012.04.056

Huang YJ, Tao YL, Lin J, Shang-Guan ZH (2009) Annual cycle of gross β activities in aerosol around Daya Bay area, China. Chemosphere 75:929–933. https://doi.org/10.1016/j.chemosphere.2009.01.022

Jie M, Xiaolei J, Xiaorui S, Li Y, he Hui KY (2017) Physical condition and development trend of 3~6 year old collective children in Beijing(Chinese). Matern Child Heal Care China 32:1–5

Jin Y, O'Connor D, Ok YS et al (2019) Assessment of sources of heavy metals in soil and dust at children's playgrounds in Beijing using GIS and multivariate statistical analysis. Environ Int 124:320–328. https://doi.org/10.1016/j.envint.2019.01.024

Jung H, Kittelson DB, Zachariah MR (2005) The influence of a cerium additive on ultrafine diesel particle emissions and kinetics of oxidation. Combust Flame 142:276–288. https://doi.org/10.1016/j.combustflame.2004.11.015

Kicinska A, Bozecki P (2018) Metals and mineral phases of dusts collected in different urban parks of Krakow and their impact on the health of city residents. Environ Geochem Health 40:473–488. https://doi.org/10.1007/s10653-017-9934-5

Kilian J, Kitazawa M (2018) The emerging risk of exposure to air pollution on cognitive decline and Alzheimer's disease – evidence from epidemiological and animal studies. Biom J 41:141–162. https://doi.org/10.1016/j.bj.2018.06.001

Kittner N, Fadadu RP, Buckley HL et al (2018) Trace metal content of coal exacerbates air-pollution-related health risks: the case of lignite coal in Kosovo. Environ Sci Technol 52:2359–2367. https://doi.org/10.1021/acs.est.7b04254

Langrish JP, Mills NL, Chan JKK et al (2009) Beneficial cardiovascular effects of reducing exposure to particulate air pollution with a simple facemask. Part Fibre Toxicol 6:1–9. https://doi.org/10.1186/1743-8977-6-8

Li Tong NS (1997) Element abundances of the continental lithosphere in China (in Chinese). Geol Prospect 33:31–37

Li J, Chen L, Xiang Y, Xu M (2018a) Research on influential factors of PM2 . 5 within the Beijing-Tianjin-Hebei Region in China. 2018:

Li M, Wu Y, Tian YH et al (2018b) Association between PM2.5 and daily hospital admissions for heart failure: a time-series analysis in Beijing. Int J Environ Res Public Health 15. https://doi.org/10.3390/ijerph15102217

Lin Y-C, Hsu S-C, CC-K C et al (2016) Wintertime haze deterioration in Beijing by industrial pollution deduced from trace metal fingerprints and enhanced health risk by heavy metals. Environ Pollut 208:284–293. https://doi.org/10.1016/j.envpol.2015.07.044

Liu Y, Li S, Sun C et al (2018) Pollution level and health risk assessment of PM 2.5 -bound metals in baoding city before and after the heating period. Int J Environ Res Public Health 15:1–17. https://doi.org/10.3390/ijerph15102286

Lyu Y, Zhang K, Chai F et al (2017) Atmospheric size-resolved trace elements in a city affected by non-ferrous metal smelting: indications of respiratory deposition and health risk. Environ Pollut 224:559–571. https://doi.org/10.1016/j.envpol.2017.02.039

Malinovsky G, Yarmoshenko I, Vasilyev A (2018) Meta-analysis of case-control studies on the relationship between lung cancer and indoor radon exposure. Radiat Environ Biophys 0:0. https://doi.org/10.1007/s00411-018-0770-5

Megido L, Suarez-Pena B, Negral L et al (2017) Suburban air quality: human health hazard assessment of potentially toxic elements in PM10. Chemosphere 177:284–291. https://doi.org/10.1016/j.chemosphere.2017.03.009

Men C, Liu R, Xu F et al (2018) Pollution characteristics, risk assessment, and source apportionment of heavy metals in road dust in Beijing, China. Sci Total Environ 612:138–147. https://doi.org/10.1016/j.scitotenv.2017.08.123

Miller CM, Anderson IE, Smith JF (1994) A viable tin-lead solder substitute: Sn-Ag-Cu. J Electron Mater 23:595–601. https://doi.org/10.1007/BF02653344

Ministry of Environmental Protection (China) (2012) GB 3095—2012 Ambient air quality standards(in Chinese)

Morishita M, Bard RL, Kaciroti N et al (2015) Exploration of the composition and sources of urban fine particulate matter associated with same-day cardiovascular health effects in Dearborn, Michigan. J Expo Sci Environ Epidemiol 25:145–152. https://doi.org/10.1038/jes.2014.35

Mostofsky E, Schwartz J, Coull BA et al (2012) Modeling the association between particle constituents of air pollution and health outcomes. Am J Epidemiol 176:317–326. https://doi.org/10.1093/aje/kws018

Nischkauer W, Izmer A, Neouze M-A et al (2017) Combining dispersed particle extraction with dried-droplet laser ablation ICP-MS for determining platinum in airborne particulate matter. Appl Spectrosc 71:1613–1620. https://doi.org/10.1177/0003702817693240

Padoan E, Malandrino M, Giacomino A et al (2016) Spatial distribution and potential sources of trace elements in PM10 monitored in urban and rural sites of Piedmont Region. Chemosphere 145:495–507. https://doi.org/10.1016/j.chemosphere.2015.11.094

Rich DQ, Kipen HM, Huang W et al (2012) Association between changes in air pollution levels during the Beijing olympics and biomarkers of inflammation and thrombosis in healthy young adults. JAMA - J Am Med Assoc 307:2068–2078. https://doi.org/10.1001/jama.2012.3488

Shao L, Hu Y, Shen R et al (2017) Seasonal variation of particle-induced oxidative potential of airborne particulate matter in Beijing. Sci Total Environ 579:1152–1160. https://doi.org/10.1016/j.scitotenv.2016.11.094

Sun Y, Hu X, Wu J et al (2014a) Fractionation and health risks of atmospheric particle-bound As and heavy metals in summer and winter. Sci Total Environ 493:487–494. https://doi.org/10.1016/j.scitotenv.2014.06.017

Sun Z, Shao L, Mu Y, Hu Y (2014b) Oxidative capacities of size-segregated haze particles in a residential area of Beijing. J Environ Sci (China) 26:167–174. https://doi.org/10.1016/S1001-0742(13)60394-0

Taylor S.R. (1964) Abundance of chemical elements in the continental crust : a new table. Geochim Cosmochim Acta 28:1273–1285

Thakur P, Mulholland GP (2011) Monitoring of gross alpha, gross beta and actinides activities in exhaust air released from the waste isolation pilot plant. Appl Radiat Isot 69:1307–1312. https://doi.org/10.1016/j.apradiso.2011.04.012

The People's Government of Beijing Municipality (2018) Statistical yearbook 2018 (in Chiness) (Accessed Auguest 19, 2019). In: http://www.ebeijing.gov.cn/BeijingInfo2019/Facts/t1573002.htm

Tian HZ, Wang Y, Xue ZG et al (2010) Trend and characteristics of atmospheric emissions of Hg, As, and Se from coal combustion in China, 1980-2007. Atmos Chem Phys 10:11905–11919. https://doi.org/10.5194/acp-10-11905-2010

Tzortzis M, Tsertos H (2004) Determination of thorium, uranium and potassium elemental concentrations in surface soils in Cyprus. J Environ Radioact 77:325–338. https://doi.org/10.1016/j.jenvrad.2004.03.014

U.S. EPA (1989) Risk assessment guidance for superfund volume I human health evaluation manual (Part A). Off Emerg Remedial Response 1:1–291

U.S. EPA (2001) Risk assessment guidance for superfund (RAGS) Volume III(Part A)

U.S. EPA (2004) Risk assessment guidance for superfund (RAGS). Volume I. Human health evaluation manual (HHEM). Part E.

U.S. EPA (2007) Lead: human exposure and health risk assessments for selected case studies volume I. Human exposure and health risk assessments. I:

U.S. EPA (2009) Risk assessment guidance for superfund volume I: human health evaluation manual (Part F)

U.S. EPA (2011) Exposure Factors Handbook

U.S. EPA (2014) Recommended default exposure factors. https://rais.ornl.gov/documents/EFH_Table.pdf (Accessed Auguest 3, 2019)

U.S. EPA (2016) Initial list of hazardous air pollutants (Accessed Auguest 23, 2019). In: https://www.epa.gov/haps/initial-list-hazardous-air-pollutants-modifications#mods

U.S. EPA 2019 Basic Information about lead air pollution.https://www.epa.gov/lead-air-pollution/basic-information-about-lead-air-pollution#health (Accessed Auguest 3, 2019). In: https://www.epa.gov/lead-air-pollution/basic-information-about-lead-air-pollution#health

U.S. EPA (2019a) Health effects notebook for hazardous air pollutants(Accessed Auguest 12, 2019). In: https://www.epa.gov/haps/health-effects-notebook-hazardous-air-pollutants

U.S. EPA (2019b) Regional screening levels (RSLs)-generic tables (Accessed Auguest 24, 2019). In: https://www.epa.gov/risk/regional-screening-levels-rsls-users-guide

U.S.EPA (2010) Health effects notebook for hazardous air pollutants. In: https://www.epa.gov/haps/health-effects-notebook-hazardous-air-pollutants

UNEP, 2010. Final review of scientific information on lead. https://wedocs.unep.org/bitstream/handle/20.500.11822/27635/LeadRev.pdf?sequence=1&isAllowed=y. Accessed 1 Aug 2019.

UNEP (2019) A review of 20 years' air pollution control in Beijing

UNSCEAR (2000) Sources and Effects of Ionizing Radiation.

Valavanidis A, Fiotakis K, Vlahogianni T et al (2006) Characterization of atmospheric particulates, particle-bound transition metals and polycyclic aromatic hydrocarbons of urban air in the centre of Athens (Greece). Chemosphere 65:760–768. https://doi.org/10.1016/j.chemosphere.2006.03.052

Van Leeuwen FXR (2002) A European perspective on hazardous air pollutants. Toxicology 181–182:355–359. https://doi.org/10.1016/S0300-483X(02)00463-8

Vik EA, Breedveld G, Farestveit T, et al (1999) Guidelines for the risk assessment of contaminated sites

Wei X, Gao B, Wang P et al (2015) Pollution characteristics and health risk assessment of heavy metals in street dusts from different functional areas in Beijing, China. Ecotoxicol Environ Saf 112:186–192. https://doi.org/10.1016/j.ecoenv.2014.11.005

WHO (2000) Air quality guidelines for Europe.

WHO (2013a) Review of evidence on health aspects of air pollution – REVIHAAP Project

WHO (2013b) Health effects of particulate matter: policy implications for countries in eastern Europe, Caucasus and central Asia

WHO (2017) Evolution of WHO air quality guidelines: past, present and future

Yang H, Tao W, Liu Y et al (2019) The contribution of the Beijing, Tianjin and Hebei region's iron and steel industry to local air pollution in winter. Environ Pollut 245:1095–1106. https://doi.org/10.1016/j.envpol.2018.11.088

Yao PH, Shyu GS, Chang YF et al (2015) Lead isotope characterization of petroleum fuels in Taipei, Taiwan. Int J Environ Res Public Health 12:4602–4616. https://doi.org/10.3390/ijerph120504602

Yue W, Tong L, Liu X et al (2019) Short term Pm2.5 exposure caused a robust lung inflammation, vascular remodeling, and exacerbated transition from left ventricular failure to right ventricular hypertrophy. Redox Biol 22:101161. https://doi.org/10.1016/j.redox.2019.101161

Zanobetti A, Franklin M, Koutrakis P, Schwartz J (2009) Fine particulate air pollution and its components in association with cause-specific emergency admissions. Environ Heal A Glob Access Sci Source 8. https://doi.org/10.1186/1476-069X-8-58

Zhang L, Jin X, Johnson AC, Giesy JP (2016) Hazard posed by metals and As in PM2.5 in air of five megacities in the Beijing-Tianjin-Hebei region of China during APEC. Environ Sci Pollut Res Int 23:17603–17612. https://doi.org/10.1007/s11356-016-6863-2

Zheng X, Zhao W, Yan X et al (2015) Pollution characteristics and health risk assessment of airborne heavy metals collected from Beijing Bus Stations. Int J Environ Res Public Health 12:9658–9671. https://doi.org/10.3390/ijerph120809658

Zong W, Xiao D, Ping LIU, et al (2009) Human exposure factors of chinese people in environmental health risk assessment. Environ Sci

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

·放射卫生·

日本福岛第一核电站事故七年后环境放射性水平与公众健康情况的现状及启示

崔力萌[1]　高村升[2]　马永忠[1]

[1]北京市预防医学研究中心 北京市疾病预防控制中心放射卫生防护所 100013；[2]长崎大学原爆后障害医疗研究所 8528523

崔力萌现在长崎大学原爆后障害医疗研究所 8528523

通信作者：马永忠，Email：myz0905@ 126.com

【摘要】　2011 年 3 月 11 日，地震和海啸袭击日本东北部，造成福岛第一核电站发生大量放射性物质释放到环境中的严重事故。本文对后福岛时期的环境监测方式、环境数据（环境 γ 剂量率、环境样品）及食品、野生动植物等监测结果进行总结分析，并归纳综述近年来福岛地区环境及灾民健康情况。通过总结福岛第一核电站事故经验，结合我国国情进行了讨论分析。

【关键词】　福岛核事故；　放射性污染；　健康管理；　去污

DOI：10. 3760/cma.j.issn.0254-5098. 2019. 08. 011

Situation and enlightenment in an environmental radioactivity and public health perspective seven years after Fukushima nuclear power plant accident

Cui Limeng[1], Noboru Takamura[2], Ma Yongzhong[1]

[1]Department of Radiation Protection, Beijing Center for Disease Prevention and Control, Beijing Research Center for Preventive Medicine, Beijing 100013, China; [2]Atomic Bomb Disease Institute, Nagasaki University, Nagasaki 8528523, Japan

Cui Limeng is working at Atomic Bomb Disease Institute, Nagasaki University, Nagasaki 8528523, Japan

Corresponding author: Ma Yongzhong, Email: myz0905@ 126.com

【Abstract】　Since the accident on March 11th 2011 at the Fukushima Daiichi Nuclear Power Station following the Great East Japan Earthquake, huge amount of radionuclide has been released to the surrounding environment. In this study, the environmental monitoring method, γ-ray dose rates, radioactivity in environmental samples, food, wild animals and plants, health situation of residents were summarized. Through summarizing the accident experience of Fukushima Daiichi Nuclear Power Station, this research discussed and analyzed the accident combining with the situation in China.

【Key words】　Fukushima nuclear accident;　Radioactive contamination;　Health management;　Decontamination

DOI：10. 3760/cma.j.issn.0254-5098. 2019. 08. 011

2011 年 3 月 11 日 14∶46，日本东北地区遭遇地震，50 min 后海啸来袭，21∶23，政府发布福岛第一核电站 3 km 半径内避难指示；3 月 12 日 5∶44 发布 10 km 半径内避难指示，15∶36，1 号机组爆炸，18∶25 发布 20 km 半径内避难指示；3 月 14 日 11∶01，3 号机组爆炸，3 月 15 日，2 号机组合 4 号机组爆炸，发布半径 20～30 km 屋内避难指示。福岛核事故等级达到 7 级。地震时，约 78 000 人居住在核电站 20 km 范围内，62 000 人居住在 20～30 km 范围内。截至 2018 年 3 月 12 日，福岛县（相当于我国的省）死亡人数 4 051 人，损毁房屋 96 027 栋[1-2]。国际原子能辐射效应科学委员会（UNSCEAR）2013 年报告书推定向大气释放^{134}Cs（半衰期 2 年）为 9.0 PBq，^{137}Cs（半衰期 30 年）为 8.8 PBq，^{131}I（半衰期 8 d）为 120 PBq[3]。

我国迅速启动应急行动，对我国食品、饮用水、气溶胶样品进行监测及对日本入境人员进行表面污染检测，并及时与公众进行风险沟通[4]。事故后，对日本政府应急中的不足和经验教训，灾民照射水平和健康管理情况等进行了总结[5-6]。后福岛时期，张琼等[7]综述了日本灾后去污日程及方法，强调预先制定事故后恢复和治理的法规框架的重要性。各国应利用福岛事故的经验，改进和完善现有的核事故应急计划，并通过跟进其中长期的恢复过程，了解人工放射性核素的生态循环及对人群健康的危害。

目前，日本形成以政府机构与研究所、大学、医院、企业等机构合作的恢复模式。环境省（环境监测部门）、厚生劳动省（医疗卫生、社会保障的政府部门）、农林水产省（农作物

监测部门)、复兴厅及地方环境事务所等机构利用互联网持续更新数据。本文根据上述网站公布的数据(数据来源多为政府在各个地方设置的检查站和大学等学术机构)以及近年关于福岛地区的英文学术论文进行总结综述。

一、环境动态

事故前,福岛县环境 γ 剂量率本底范围为 0.07~0.12 μSv/h[8]。事故后,政府免费向居民出借 γ 剂量率检测仪器,并对学校、儿童活动区、景点、公共场所等特定场所进行集中监测。截至 2017 年 2 月,福岛县在公共场所设置固定 γ 剂量率监测仪器(探测地上 1 m)628 台;在儿童可能活动的场所设置适用于儿童的 γ 剂量率监测仪(探测地上 50 cm及1 m)3 099 台[9]。2017 年 4 月至 7 月,在居民返回区域,地上 1 m 高处环境 γ 剂量率的均值为(0.13 ± 0.11)μSv/h、范围在 0.04~1.50 μSv/h 之间[10]。

除固定点位监测外,还使用直升机、移动车辆和步行相合的方式进行高密度、高覆盖、高频率的环境 γ 剂量率调查。直升机可在海上和地势复杂区域进行监测[11];车载剂量率仪器则用来测定污染范围及变化趋势[12];在居民结束避难返乡区域,利用步行调查寻找污染地区及估算居民在该地区生活的年剂量[13]。由于污染情况受天气及人类干预等因素影响,同一村庄、院落内污染程度也可能有很大不同[14-15],因此应进行长期监测,发现污染区域尽快去污,避免不必要的照射。

林业为福岛县主要产业(约 50%阔叶林,40%针叶林,剩余为竹林等),目前在树干、树液、新鲜落叶中均仍能发现较高浓度放射性铯[16]。通过修剪树枝、移除土壤等去污方式,2016 年 3 月,森林中环境 γ 剂量率大于 1 μSv/h 的区域减少到了 7%[17]。然而,Ayabe 等[18]指出,由于树叶的不断凋落,放射性铯仍在不断从树冠转移到地面,因此森林去污是无效的。有研究指出,放射性核素正逐渐向下层土壤迁移[19-20],且迁移速度快于切尔诺贝利地区[21-22]。目前,90%放射性铯主要存在于地表 10 cm 范围[19,23]。

截至 2017 年 9 月,日本参与去污人次达到 1 800 万人次,共除去土壤、废弃物合计 16 500 km^3。放射性废弃物首先放置于临时储存场,然后运送至中长期储藏地点,预计储存时间为 30 年[24]。

表 1 列出部分自然环境样品检测结果。在去污难度较大的河泥、湖泥中均检测到浓度较高的人工放射性核素,这同时会导致鱼类污染。地下水的污染目前尚不明显,但一些井水样品中检测到微量的放射性核素,因此持续检测仍旧是必要的。

二、水、食品及野生动植物监测结果

目前日本实行的食品标准为,放射性铯浓度(^{134}Cs+^{137}Cs)应低于:普通食品(100 Bq/kg)、牛奶(50 Bq/kg)、婴幼儿食品(50 Bq/kg)、饮用水(10 Bq/kg)[30]。近期该国政府公布的结果(表 2)可见,饮用水、大米、蔬菜、肉类、牛奶及栽培菌菇中的放射性活度均符合标准。但在野生动植物中检测到了较高的放射性铯活度。

有研究综述了福岛县菌菇样品结果,指出进入市场前的菌菇样品 2.7%~4.8%超出限值,进入市场后则为 0.6%~0.7%[39]。2015 年,川内村(事故 20 km 范围内)采集的野生菌菇中有 77.3%超出 100 Bq/kg,观测到^{134}Cs 活度的下降趋势,未观测到^{137}Cs 活度的下降趋势[35]。野生菌菇作为生态环境中的分解者,可以浓集大量放射性铯,因此在核事故后应仅在检测后进行选择性食用。

福岛县各乡镇中设有食品放射性核素无损检测设备,如居民带来的食物中放射性铯活度未超出限值,仍可带回家食用。同时使用高纯锗 γ 谱仪对居民提供的食品、饮用水等样品进行检测。对学校提供的食物进行每日抽检并在互联网公布结果。

三、人群健康与科普

2011 年 3 月 11 日,福岛县共有居民 2 024 401 人,事故发生后,共有 164 865 人离开家乡避难。截至 2019 年 1 月,仍有 42 104 人未返回家乡[2]。2017 年 4 月,浪江町、饭馆村、富冈町的部分区域解除避难指示和居住限制,居民开始返回[40]。然而,由于医疗服务、学校等公共服务设施不足、缺少就业岗位、担心辐射危害等原因,截至 2019 年 2 月,富冈町仅 864 人返回,占居民总数 6.6%[41]。

2011 年 6 月—2019 年 1 月,338 366 人进行了全身计数器检查[42-43],14 人>1 mSv,10 人>2 mSv,2 人>3 mSv。由于切尔诺贝利核事故后儿童甲状腺癌症发病率的上升[44],核事故后该地区展开了甲状腺疾病筛查工作。2011—2013 年

表 1 福岛县部分自然环境样品监测结果

Table 1 Radioactivity in environment samples from Fukushima prefecture

样品种类	时间	地点	样本数	^{134}Cs	^{137}Cs
河水	2017 年[25]	福岛县	326	ND	ND~0.75 Bq/L
河泥	2017 年[25]	福岛县	326	ND~720 Bq/kg	ND~6 000 Bq/ kg
湖水(水源地)	2017 年[25]	福岛县	306	ND~1.5 Bq/L	ND~15 Bq/L
湖泥	2017 年[25]	福岛县	210	ND~41 kBq/ kg	2.5~320 kBq/kg
湖泥	2014—2015 年[26]	福岛县真野大坝	25	28~40 kBq/kg(平均值范围)	
地下水	2018.5—2018.6[27]	福岛县	225	ND	ND
井水	2014—2016 年[28]	福岛县南相马市	11	-	ND~26.7 mBq/L
雨水	2018.4—2018.11[29]	福岛县福岛市	64	ND	ND~5.45 mBq/L

注:ND.小于探测下限;“-”为未测量

表 2　福岛地区部分饮用水、食品及野生动物调查结果

Table 2　Radioactivity in drinking water, food and wild animal samples from Fukushima prefecture

样品种类	日期	数量	$^{134}Cs+^{137}Cs$(Bq/kg)
饮用水[31]	2019.1	755	ND
大米[32]	2018.8—2019.3	9 175 336	<50
蔬菜[33]	2018.2—2019.2	1 454	ND ~40
肉类[33]	2018.2—2019.2	3 792	ND ~12.8
牛奶[33]	2018.2—2019.2	350	ND
海鱼[34]	2018.4—2019.2	6 326	ND ~220
栽培菌菇[33]	2018.2—2019.2	1 426	ND ~85.9
野生菌菇[35]	2015	159	ND ~5 600
养殖鱼[33]	2018.2—2019.2	7 444	ND ~195
无脊椎动物(蚯蚓)[36]	2017	33	3 400 ~19 000
两栖类(海龟)[36]	2017	3	1 900 ~11 000
鼠类[36]	2017	18	1 100 ~29 000
鸟类(燕子)[36]	2017	10	30 ~400
野猪[37]	2019	7	110 ~9 400
野猪[38]	2011—2016	1 033	900 ±2 743

注:ND.小于探测下限

度,对福岛县 300 473 人进行了甲状腺疾病筛查,乳头状癌 100 人;2014—2015 年度,筛查 270 511 人,甲状腺乳头状癌 43 人;2016—2017 年度,检查 191 669 人,甲状腺乳头状癌 7 人。目前为止福岛地区儿童甲状腺结节和囊肿发生率未见明显增加[45],若首次检查未发现甲状腺相关疾病,2 年或 5 年后再次筛查。

为应对灾民出现的抑郁、创伤后应激障碍、过度饮酒等问题[46],福岛县设置了 6 个心理疾病中心,7 个保健中心。定期进行健康讲座、心理咨询及健康体检等活动,并进行大量问卷调查,内容包括放射防护知识、家庭状况、心理健康、返乡意愿等[47-49]。调查显示,事故后居民的平均腰围增长 1 cm,体重增长 3 kg,代谢综合征、空腹血糖水平也有所增加[50]。

日本在事故后广泛面向群众开展辐射知识科普,放射知识科普读物区分为小学低年级,小学高年级及中学,中学生以上 3 个年龄段,并出版了英语版本[16];对核事故地区和核电站周边中小学教师进行辐射知识培训;设置电台、手机应用等进行辐射知识讲解;同时在每个村镇设置辐射防护相关知识咨询员等。

四、讨论

对比 2011 年,由于去污工作的持续进行及短半衰期核素的物理衰变,福岛地区居住环境中 γ 剂量率有了显著下降。根据其发布的监测结果,居民归还区域大部分已经恢复到事故前本底水平。在禁止进入区域,去污工作的持续进行使很多区域的解除封锁列入日程,但在中长期污染物贮存场,仍需要 30 年或更长的时间来恢复。食物和饮用水监测结果显示,居民通过本地食物摄入放射性核素的概率较低,不被认为会增加终生癌症发生率,但持续的食品监测是有必要的。

对于大部分区域被森林覆盖的福岛县,放射性铯在森林系统中较长生态半衰期导致了野生的动植物中人工放射性核素超过标准限值,发生核事故时应避免食用野生动植物,事故后应仅在检测并确认安全后食用。森林放射生态学、海洋放射生态学等与核事故恢复相结合的研究是必要的。

受灾民众逐渐选择结束避难返乡,与其各级机构采取的医疗保健、风险沟通方式等密切相关。医疗健康方面,对于事故时儿童群体,甲状腺疾病等仍需持续关注和队列研究。对于累积剂量较高的受灾群众,其后代的表观遗传学研究也是有必要的。通过对不同人群的放射防护知识普及和双向沟通,公众正在缓慢的恢复对权威机构信任。借鉴其经验,我国权威机构在风险沟通中应避免福岛事故应急阶段发生的专家口径不一致,如过度使用专有名词和使用不同辐射单位进行风险沟通等情况。后福岛时期,由于返乡居民较少,其权威机构和专家能够做到小组及深度访谈、入户检测、日常食品检测等。与大多数国家情况相同,我国灾后支援队伍中心理救援人员仍旧不足,因此对于应急人员的风险沟通培训和心理救援人员的辐射知识培训也是必要的。

我国人口较多且居住密集,核应急培训及演练难度较大。在互联网时代,通过社交网络对公众进行知识科普,可做到较强的覆盖广度。对中小学生进行辐射知识科普同样是值得参考的模式。需要注意的是,核事故时,电视、互联网、电话均可能无法使用,因此使公众熟悉避难地点位置、稳定性碘领取地点、服用时间及方式等非常重要。我们应当借鉴福岛事故经验,避免同样的错误,如将低剂量区域群众疏散到了高剂量地区、未能及时发放碘片等。近年来,各核电站积极开展核应急演练与培训,与国际组织合作和沟通,对公众开放核电站参观等,已取得积极的成效。与日本不同,我国核应急体系具备军民融合的特点,应当同时借鉴切尔诺贝利核事故的经验,加强应急救援人员辐射救援知识培训,避免辐射事故,保障公众和工作人员的安全。

利益冲突　本研究由署名作者按以下贡献声明独立开展,未接受有关公司的任何赞助,不涉及各相关方的利益冲突

作者贡献声明　崔力萌负责文献整理阅读及文章撰写;高村升负责文章内容指导;马永忠负责整体设计和审阅

参 考 文 献

[1] The official website of Fukushima Prefecture. 平成 23 年東北地方太平洋沖地震による被害状況即報[EB/OL]. 2018[2019-3-5]. http:// www. pref. fukushima. lg. jp/site/portal/list281-896.html.

[2] Fukushima Revitalization Station. ふくしま復興のあゆみ[EB/OL]. 2018[2018-2-28]. http:// www.pref. fukushima.lg.jp/site/portal/.

[3] United Nations Scientific Committee on the Effects of Atomic Radiation. Sources and effects of ionizing radiation[R]. Vienna: United Nations, 2013.

[4] 苏旭,孙全富. 日本福岛第一核电站事故的卫生应对[J]. 中华放射医学与防护杂志,2012, 32 (2): 113-115. DOI:10. 3760/cma.j.issn.0254-5098. 2012. 02. 001.
Su X, Sun QF. Hygienic response to the Fukushima Daiichi nuclear power plant accident in Japan[J]. Chin J Radiol Med Prot, 2012, 32 (2): 113-115. DOI: 10. 3760/cma. j. issn. 0254-5098. 2012. 02. 001.

[5] 徐卸古,甄蓓,杨晓明,等. 日本福岛核电站核事故应急处置的经验和教训[J].军事医学, 2012, (12): 889-892.
Xu XG, Zhen B, Yang XM, et al. Experience and lessons of nuclear accident emergency disposal at Fukushima Nuclear Power Station in Japan[J]. Mil Med, 2012, 36 (12): 889-892.

[6] 刘长安,李小娟,陈尔东. 福岛核事故受影响居民的照射水平评估和健康管理调查[J]. 中华放射医学与防护, 2012, 32 (5): 541-547. DOI: 10. 3760/cma. j. issn. 0254-5098. 2012. 05. 027.
Liu CA, Li XJ, Chen ED. Assessment of exposure level and health management survey of the residents affected by Fukushima Nuclear Accident[J]. Chin J Radiol Med Prot, 2012, 32(5): 541-547. DOI: 10. 3760/cma.j.issn.0254-5098. 2012. 05. 027.

[7] 张琼,王博,王亮,等.福岛核事故场外环境修复综述及启示[J]. 辐射防护, 2017, 37(3): 240-247.
Zhang Q, Wang B, Wang L, et al. Overview and enlightenment of outside environmental restoration in Fukushima Nuclear Accident [J]. Radiat Prot, 2017, 37 (3): 240-247.

[8] Abe S, Fujitaka K, Abe M, et al. Extensive field survey of natural radiation in Japan[J]. J Nucl Sci Technol, 1981, 18 (1): 21-45. DOI:10. 1080/18811248. 1981. 9733221.

[9] The Official Website of Fukushima Prefecture. 放射線のモニタリング[EB/OL]. http://www. pref. fukushima. lg. jp/site/portal/list272-851.html, 2018.

[10] Japan Atomic Energy Agency. 福島県環境放射線モニタリング・メッシュ調査(第 10 回)結果[EB/OL].2017[2017-9-11]. https://emdb. jaea. go. jp/emdb/assets/site _ data/ja/associated/1010117010/mesh-10-zentai.pdf.

[11] Sanada Y, Orita T, Torii T. Temporal variation of dose rate distribution around the Fukushima Daiichi nuclear power station using unmanned helicopter[J]. Appl Radiat Isot, 2016, 118(8): 308-316. DOI:10. 1016/j.apradiso.2016. 09. 008.

[12] Andoh M, Mikami S, Tsuda S, et al. Decreasing trend of ambient dose equivalent rates over a wide area in eastern Japan until 2016 evaluated by car-borne surveys using KURAMA systems[J]. J Environ Radioact, 2018, 192: 385-398. DOI: 10. 1016/j. jenvrad.2018. 07. 009.

[13] Andoh M, Yamamoto H, Kanno T, et al. Measurement of ambient dose equivalent rates by walk survey around Fukushima Dai-ichi Nuclear Power Plant using KURAMA-II until 2016[J]. J Environ Radioact, 2018, 190-191: 111-121. DOI: 10. 1016/j. jenvrad. 2018. 04. 025.

[14] Wainwright HM, Seki A, Chen J, et al. A multiscale bayesian data integration approach for mapping air dose rates around the Fukushima Daiichi Nuclear Power Plant[J]. J Environ Radioact, 2017, 167: 62-69. DOI: 10. 1016/j.jenvrad.2016. 11. 033.

[15] Wainwright HM, Seki A, Mikami S, et al. Characterizing regional-scale temporal evolution of air dose rates after the Fukushima Daiichi Nuclear Power Plant accident[J]. J Environ Radioact, 2018, 189: 213-220. DOI:10. 1016/j.jenvrad.2018. 04. 006.

[16] Kato H, Onda Y, Saidin ZH, et al. Six-year monitoring study of radiocesium transfer in forest environments following the Fukushima nuclear power plant accident[J]. J Environ Radioact, 2018, in press. DOI:10. 1016/j.jenvrad.2018. 09. 015.

[17] Tsuruta T, Niizato T, Nakanishi T, et al. Status of study of long-term assessment of transport of radioactive contaminants in the environment of Fukushima-as a part of dissemination of evidence-based information-October 2017 Japan Atomic Energy Agency[R]. Ibaraki: JAEA, 2017:50. DOI:10. 11484/jaea-review-2017-018.

[18] Ayabe Y, Hijii N, Takenaka C. Effects of local-scale decontamination in a secondary forest contaminated after the Fukushima nuclear power plant accident[J]. Environ Pollut, 2017, 228:344-353. DOI:10. 1016/j.envpol.2017. 05. 041.

[19] Matsuda N, Mikami S, Shimoura S, et al. Depth profiles of radioactive cesium in soil using a scraper plate over a wide area surrounding the Fukushima Dai-ichi Nuclear Power Plant, Japan [J]. J Environ Radioact, 2015, 139:427-434. DOI:10. 1016/j. jenvrad.2014. 10. 001.

[20] Lepage H, Evrard O, Onda Y, et al. Depth distribution of cesium-137 in paddy fields across the Fukushima pollution plume in 2013 [J]. J Environ Radioact, 2015, 147:157-164. DOI:10. 1016/j. jenvrad.2015. 05. 003.

[21] Konoplev A, Golosov V, Laptev G, et al. Behavior of accidentally released radiocesium in soil-water environment: Looking at Fukushima from a Chernobyl perspective[J]. J Environ Radioact, 2016, 151:568-578. DOI:10. 1016/j.jenvrad.2015. 06. 019.

[22] Takahashi J, Onda Y, Hihara D, et al. Six-year monitoring of the vertical distribution of radiocesium in three forest soils after the Fukushima Dai-ichi Nuclear Power Plant accident[J]. J Environ Radioact, 2018, 192 (5): 172-180. DOI: 10. 1016/j. jenvrad. 2018. 06. 015.

[23] City F, Rates WB. Association of the Great East Japan Earthquake and the Daiichi nuclear disaster association of the Great East Japan Earthquake and the Daiichi nuclear disaster in Fukushima city, Japan, with birth rates[J]. 2019, 2(1):e187455. DOI:10. 1001/jamanetworkopen.2018. 7455.

[24] Ministry of the Environment. 被災地の環境再生に向けた取組の現状[EB/OL]. 2018[2018-3-2]. https://www.env.go.jp/jishin/rmp/conf/19/mat04.pdf.

[25] Ministry of the Environment. 水環境における放射性物質のモニタリング結果[EB/OL]. 2016[2016-3]. http://www.env.go.jp/air/rmcm/conf_cm2/report-h28_all.pdf.

[26] Huon S, Hayashi S, Laceby JP, et al. Source dynamics of radiocesium-contaminated particulate matter deposited in an agricultural water reservoir after the Fukushima nuclear accident [J]. Sci Total Environ, 2018, 612: 1079-1090. DOI:10. 1016/j. scitotenv.2017. 07. 205.

[27] Ministry of the Environment. 平成 29 年度公共用水域放射性物質モニタリング調査結果-福島県調査結果[EB/OL]. 2018. http://www.env.go.jp/jishin/monitoring/results_r-pw-h29.html.

[28] Shizuma K, Fujikawa Y, Kurihara M, et al. Identification and temporal decrease of (137) Cs and (134) Cs in groundwater in Minami-Soma city following the accident at the Fukushima Dai-ichi Nuclear Power Plant[J]. Environ Pollut, 2018, 234: 1-8. DOI: 10.1016/j.envpol.2017.11.018.

[29] Fukushima Prefecture. 定時降水モニタリング結果[EB/OL]. 2019 [2018-12-17]. https://www.pref.fukushima.lg.jp/site/portal/ps-teiji-kousui-kako.html.

[30] Ministry of Health, Labour and Welfare. Radioactive materials in foods[EB/OL]. 2018 [2018-3-23]. https://www.mh lw.go.jp/english/topics/2011eq/dl/food-130926_1.pdf.

[31] Ministry of Health, Labour and Welfare. 水道関連の報道発表[EB/OL]. 2018 [2018-12-7]. https://www.mhlw.go.jp/stf/kinkyu/copy_of_2r98520000016378.html.

[32] The Official Website of Fukushima Prefecture. 全量全袋検査の検査結果[EB/OL]. 2019[2019-3-1]. https:// fukumegu.org/ok/contentsV2/.

[33] Fukushima Prefecture. Forestry and fisheries products processed food monitoring information Fukushima prefeture agriculture, 福島県による農林水産物の放射性物質の検査結果 [EB/OL]. 2019[2019-2-1]. https://www.new-fukushima.jp/result.

[34] Fisheries Agency. 水産物の放射性物質調査の結果[EB/OL]. 2019 [2019-2-1]. http://www.jfa.maff.go.jp/j/ housyanou/kekka.html.

[35] Orita M, Nakashima K, Takamura N, et al. Radiocesium concentrations in wild mushrooms after the accident at the Fukushima Daiichi Nuclear Power Station: Follow-up study in Kawauchi village[J]. Sci Rep, 2017, 7 (1): 1-7. DOI:10.1038/s41598-017-05963-0.

[36] Ministry of the Environment. 野生動植物への放射線影響調査[EB/OL]. 2017 [2018-5-24]. http://www.env.go.jp/jishin/monitoring/results_r-wl.html.

[37] Labour and Welfare Ministry of Health.食品中の放射性物質の検査結果について(第 1120) [EB/OL]. 2019 [2019-3-5]. https://www.mhlw.go.jp/stf/houdou/0000212863_00033.html.

[38] Nemoto Y, Saito R, Oomachi H. Seasonal variation of Cesium-137 concentration in Asian black bear (Ursus thibetanus) and wild boar (Sus scrofa) in Fukushima Prefecture, Japan[J]. PLoS One, 2018, 13 (7): 1-14. DOI: 10.1371/journal.pone.0200797.

[39] Prand-Stritzko B, Steinhauser G. Characteristics of radiocesium contaminations in mushrooms after the Fukushima nuclear accident: evaluation of the food monitoring data from March 2011 to March 2016[J]. Environ Sci Pollut Res Int, 2018, 25 (3): 2409-2416. DOI:10.1007/s11356-017-0538-5.

[40] The Official Website of Fukushima Prefecture. 避難指示区域の状況[EB/OL].2017 [2017-3-10]. http://www.pref.fukushima.lg.jp/site/portal/list271-840.html.

[41] Tomioka Town Official Site. 県内外の避難・居住先別人数[EB/OL]. 2019 [2019-2-6]. http:// www.tomioka-town.jp/soshiki/jumin/jumin/hinansya_ninzu/2289.html.

[42] Miyazaki M. Using and explaining individual dosimetry data: case study of four municipalities in Fukushima[J]. Asia Pacif J Pub Health, 2017, 29(2S):110S-119S. DOI:10.1177/1010539517693082.

[43] Miyazaki M, Hayano R. Individual external dose monitoring of all citizens of Date City by passive dosimeter 5 to 51 months after the Fukushima NPP accident (series): II. Prediction of lifetime additional effective dose and evaluating the effect of decontamination on individual[J]. J Radiol Prot, 2017, 37 (3): 623-634. DOI:10.1088/1361-6498/aa6094.

[44] Iglesias ML, Schmidt A, Ghuzlan A, et al. Radiation exposure and thyroid cancer: a review[J]. Arch Endocrinol Metab, 2017, 61 (2): 180-187. DOI:10.1590/2359-3997000000257.

[45] 孙全富, 赵锡鹏, 李小亮.日本福岛第一核电站事故对儿童甲状腺的影响[J]. 中华放射医学与防护杂志, 2016, 36 (6): 448-452. DOI:10.3760/cma.j.issn.0254-5098.2016.06.010.
Sun QF, Zhao XP, Li XL. Effects of Fukushima Daiichi Nuclear Power Plant Accident on children's thyroid[J]. Chin J Radiol Med Prot, 2016, 36 (6): 448-452. DOI: 10.3760/cma.j.issn.0254-5098.2016.06.010.

[46] Hitoshi O, Yasumura S, Maeda M, et al. From devastation to recovery and revival in the aftermath of Fukushima's Nuclear Power Plants Accident[J]. Asia Pacif J Pub Health, 2017, 29 (2): 10s-17s. DOI:10.1177/1010539516675700.

[47] Yoshida K, Orita M, Takamura N, et al. Radiation-related anxiety among public health nurses in the Fukushima Prefecture after the accident at the Fukushima Daiichi Nuclear Power Station: a cross-sectional study [J]. BMJ Open, 2016, 6 (10): 1-6. DOI: 10.1136/bmjopen-2016-013564.

[48] Murakami M, Sato A, Matsui S, et al. Communicating with residents about risks following the Fukushima Nuclear Accident [J]. Asia-Pacif J Pub Health, 2017, 29 (2suppl): 74S-89S. DOI:10.1177/1010539516681841.

[49] Orita M, Hayashida N, Takamura N, et al. Bipolarization of risk perception about the health effects of radiation in residents after the accident at Fukushima nuclear power plant[J]. PLoS One, 2015, 10 (6): 1-9. DOI:10.1371/journal.pone.0129227.

[50] Hashimoto S, Nagai M, Abe M, et al. Influence of post-disaster evacuation on oncidence of metabolic syndrome[J]. J Atheroscler Thromb, 2017, 24 (3): 327-337. DOI:10.5551/jat.35824.

(收稿日期: 2019-03-08)

www.nature.com/scientificreports

SCIENTIFIC REPORTS

natureresearch

Check for updates

OPEN

Environmental Remediation of the difficult-to-return zone in Tomioka Town, Fukushima Prefecture

Limeng Cui, Yasuyuki Taira✉, Masahiko Matsuo, Makiko Orita, Yumiko Yamada & Noboru Takamura

Temporal variations in ambient dose rates in a restricted area designated as "difficult-to-return" for residents of Tomioka Town, Fukushima Prefecture were evaluated in a car-borne survey during 2018–2019. The median dose rates in the "Decontaminated area" in the difficult-to-return zone decreased rapidly from 1.0 μSv/h to 0.32 μSv/h; however, the median dose rates in the "Non-decontaminated area" and "Radioactive waste storage area" fluctuated between 1.1–1.4 μSv/h and 0.46–0.61 μSv/h, respectively. The detected rate of the cesium-137 (^{137}Cs) (^{137}Cs-detected points per all measuring points) in the "Decontaminated area" also decreased rapidly from 64% to 6.7%, accompany with decreasing in ambient dose rates. On the other hand, the detection of ^{137}Cs in the "Radioactive waste storage area" and "Non-decontaminated area" decreased from 53% to 17% and 93% to 88%, respectively. We confirmed that the dose rates in the Decontaminated area dramatically decreased due to decontamination work aiming to help residents return home. Moreover, the estimated external exposure dose of workers during the present survey was 0.66 mSv/y in the Decontaminated area and 0.55 mSv/y in the Radioactive waste storage area, respectively. This case of Tomioka Town within the "difficult-to-return zone" may be the first reconstruction model for evaluating environmental contamination and radiation exposure dose rates due to artificial radionuclides derived from the nuclear disaster.

The Great East Japan Earthquake (magnitude 9.0) and subsequent tsunami on March 11, 2011 caused an accident at the Fukushima Daiichi Nuclear Power Station (FDNPS) that resulted in various radionuclides including cesium-134 (^{134}Cs), cesium-137 (^{137}Cs) and iodine-131(^{131}I) being released into the atmosphere and eventually depositing on land and at sea in the surrounding areas[1]. The United Nations Scientific Committee on the Effects of Atomic Radiation estimated the total release of ^{134}Cs (half-life: 2.1 y), ^{137}Cs (half-life: 30 y) and ^{131}I (half-life: 8 d) to be 9.0, 8.8 and 120.0 petabecquerels (PBq), respectively[1]. The Japanese government, municipalities and private companies have carried out environmental and individual radiation monitoring programs to confirm the radiation levels in the affected areas[2,3]. More than 8 years have passed since the accident and it has been confirmed that artificial radionuclides with a relatively long half-life such as ^{134}Cs and ^{137}Cs still exist in soil and plant samples collected around the FDNPS[1–3].

Environmental monitoring in Fukushima Prefecture have been carried out by many methods (the airborne survey by monitor stations and personnel, vehicle-borne survey, aerial-vehicle survey and radionuclide analysis of the environmental samples such as soils, sediments and foodstuffs)[3–9]. These surveys and the collected data are extremely important to precise evaluation of environmental remediation in the affected areas. Following the FDNPS accident, residential areas, farmlands, forests close to residential areas, and roads within the evacuation order areas were extensively decontaminated by March 19, 2018. This excluded an area designated as "difficult-to-return" for residents, an area in which entry and lodging are basically still prohibited[10]. According to the *Act on Special Measures for the Reconstruction and Revitalization of Fukushima* outlined in 2017, six municipalities, including Tomioka Town, are making plans to construct a Special Reconstruction and Revitalization Base aiming to lift evacuation orders and allow the residents to return to home[10].

The National government established areas estimated more than 50 mSv/y in the annual cumulative dose, as of March 2012 as the difficult-to-return zone. Tomioka Town was rearranged into a residential zone

Department of Global Health, Medicine and Welfare, Atomic Bomb Disease Institute, Nagasaki University Graduate School of Biomedical Sciences, 1-12-4 Sakamoto, Nagasaki City, Nagasaki Prefecture, 852-8523, Japan. ✉e-mail: y-taira@nagasaki-u.ac.jp

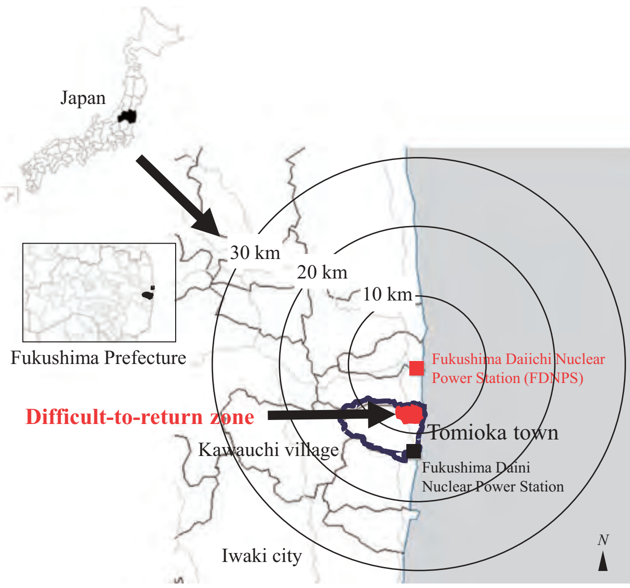

Figure 1. Location of Tomioka Town, Fukushima Prefecture, Japan. The second author (Y.T.) created the map using GIS software (Green Map III, Tokyo Syoseki, Tokyo, Japan. https://shop.tokyo-shoseki.co.jp/map). Reprinted from Green Map III under a CC BY license, with permission from Tokyo Shoseki Co., Ltd.; original copyright 2003.

and the difficult-to-return zone depending on contrasted levels of the annual cumulative dose (Fig. 1). The difficult-to-return zone is about 8.5 km^2 and about 4,800 people were living there before the disaster[11].

Long-term environmental monitoring as well as further decontamination efforts should continue around the FDNPS, including Tomioka Town. On the other hand, the external exposure level and the decontamination effects on landscape within the difficult-to-return zone have not been evaluated concretely, although data from the literature, databases and websites have been reported by the national and local governments[4–9,12,13]. Especially, recent reports on the decontamination effect on landscape are not sufficiently published[14].

Therefore, in the present study, we carried out a detailed and high-frequency radiation monitoring program using a car-borne survey to provide relatively high-density data. We also evaluated the effects of decontamination efforts, such as reductions in ambient and radiocesium dose rates, in three areas ("Decontaminated area", "Radioactive waste storage area" and "Non-decontaminated area") with markedly different characteristics in the difficult-to-return zone in Tomioka Town.

Results

Ambient dose rates. The frequency distributions of the ambient dose rates within the difficult-to-return zone of Tomioka town were illustrated in Fig. 2. In the decontaminated area, the proportion of the locations with dose rates more than 0.95 μSv/h largely dropped from 59.2% in July 2018 to 0% in July 2019. The dose rates mainly concentrated range from 0.38 to 0.95 μSv/h (61%-81%) in the radioactive waste storage area. In the non-decontaminated area, from 72% to 93% measurement points were higher than 0.95 μSv/h during the research period.

Relatively higher dose rates were observed in the Non-decontaminated area with median dose rates ranging from 1.1 to 1.4 μSv/h during the research period (Table 1). Likewise, the median dose rates ranged from 0.46 to 0.61 μSv/h in the Radioactive waste storage area. On the other hand, the ambient dose rates of the Decontaminated area dramatically decreased from 1.0 μSv/h in July 2018 to 0.32 μSv/h in July 2019. On the basis of the slope of the regression line, ambient dose rates in the last surveys decreased to 28.1%, 78.9% and 72.1% of those in the first surveys in the Decontaminated area, Radioactive waste storage area and Non-decontaminated area, respectively (Table 1).

Ambient dose rates were significantly higher in the Non-decontaminated area than in the other two areas ($p < 0.001$). In the surveys during 2018 and on January 24, 2019, the dose rates in the Decontaminated area were significantly higher than those in Radioactive waste storage area ($p < 0.001$). However, in the survey on January 12, 2019 and the four surveys after March 2019, the statistical results indicated the dose rates in the Decontaminated area fell below those of the Radioactive waste storage area ($p < 0.001$).

Furthermore, we analyzed the spectrum of the ambient gamma-ray flux (mainly artificial radionuclides such as radiocesium) using the Radi-probe system. The proportion of measurement points where radionuclides could be detected compared to all measurement points is shown in Fig. 3. The number of be detected points of ^{137}Cs ranged from 64% (588 in 922 points) to 6.7% (80 in 1188 points), 53% (313 in 592 points) to 17% (98 in 586 points) and 93% (148 in 159 points) to 88% (121 in 138 points) in the Decontaminated area, Radioactive waste storage area, and Non-decontaminated area, respectively, and those of ^{134}Cs ranged from 63% (579 in 922 points) to 3.8% (45 in 1188 points), 44% (260 in 592 points) to 10% (57 in 586 points), 89% (142 in 159 points) to 83% (114 in 138 points), respectively (Fig. 3). In the present study, radiocesium fallout driven from the FDNPS

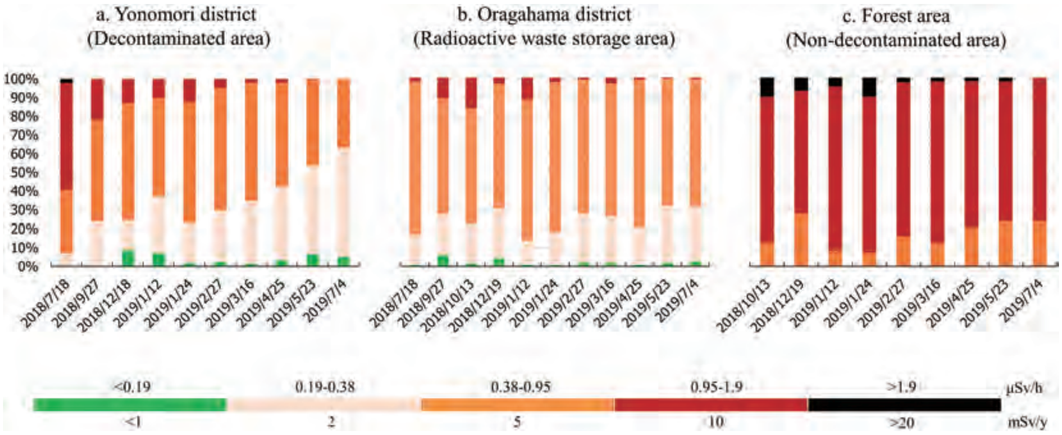

Figure 2. Relative frequencies of ambient dose rates in the Difficult-to-return zone in Tomioka Town, Fukushima Prefecture from July 2018 to July 2019. (**a**) Yonomori District (Decontaminated area); (**b**) Oragahama District (Radioactive waste storage area); (**c**) Forest area (Non-decontaminated area).

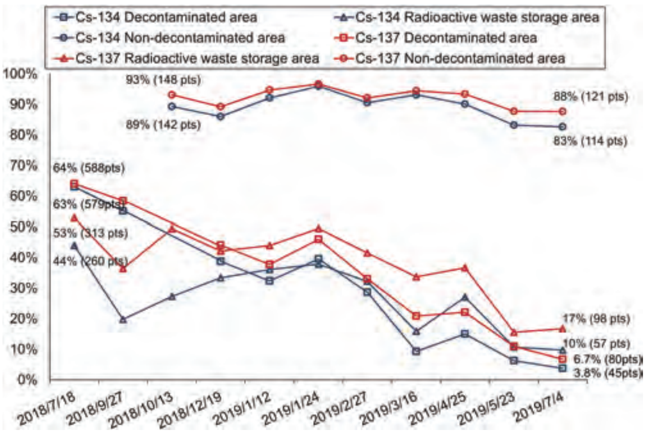

Figure 3. Proportion of localities where radiocesium could be detected in the Difficult-to-return zone in Tomioka Town from July 2018 to July 2019. Percentage is shown to the rate of detected points.

	Yonomori district (Decontaminated area)			Oragahama district (Radioactive waste storage area)			Forest area (Non-decontaminated area)		
	Points[a]	Median(min-max) (µSv/h)	Decreasing proportion (%)	Points	Median(min-max) (µSv/h)	Decreasing proportion (%)	Points	Median(min-max) (µSv/h)	Decreasing proportion (%)
2018/7/18	922	1.0 (0.24–2.82)	100	592	0.54 (0.15–1.1)	100	N/A[b]	N/A	N/A
2018/9/27	748	0.70 (0.19–1.3)	56.7	622	0.59 (0.11–1.1)	91.1	N/A	N/A	N/A
2018/10/13	N/A	N/A	N/A	510	0.55 (0.13–1.8)	109.5	159	1.4 (0.43–2.4)	100
2018/12/19	1034	0.57 (0.13–1.3)	49.6	638	0.54 (0.12–1.9)	91.5	157	1.2 (0.39–2.4)	80.4
2019/1/12	1408	0.53 (0.14–1.5)	44.6	744	0.61 (0.17–1.7)	106.6	189	1.4 (0.53–2.7)	92.8
2019/1/24	942	0.62 (0.15–1.5)	49.6	600	0.57 (0.15–1.2)	95.3	148	1.4 (0.52–2.6)	93.3
2019/2/27	826	0.51 (0.13–1.4)	42.8	525	0.50 (0.14–1.0)	85.5	127	1.3 (0.40–2.2)	85.4
2019/3/16	1508	0.46 (0.14–1.5)	37.7	849	0.51 (0.12–1.3)	85.4	145	1.3 (0.43–2.2)	79.4
2019/4/25	1187	0.41 (0.12–1.5)	39.2	725	0.52 (0.14–1.2)	84.0	121	1.3 (0.44–2.0)	79.7
2019/5/23	1102	0.36 (0.12–1.1)	35.0	597	0.46 (0.16–1.0)	76.9	155	1.1 (0.38–2.1)	73.1
2019/7/4	1188	0.32 (0.12–0.94)	28.1	586	0.46 (0.13–1.2)	78.9	138	1.1 (0.39–1.8)	72.1

Table 1. Ambient dose rates in the three districts of the Difficult-to-return zone in Tomioka Town from July 2018 to July 2019. [a]measurement points. [b]unable to survey.

accident was clearly detected by this car-borne survey system as one source of the ambient dose rate, even after 8 years from the Accident.

External effective doses. We calculated the annual external effective doses of decontamination workers and estimated that the median doses from July 2018 to July 2019 were 0.66 mSv/y for those working in the Decontaminated area and 0.55 mSv/y in the Radioactive waste storage area, respectively. Also, for residents who are going to return to the Decontaminated area, on the basis of the ambient rates in July 2019, we estimated that the median external effective dose of indoor workers was 0.69 mSv/y and that of outdoor workers was 0.87 mSv/y, respectively.

Discussion

In the present study, the median dose rate in the whole difficult-to-return zone was 0.46 μSv/h in July 2019, which showed a clear decrease. One car-borne survey in the difficult-to-return zone of Namie Town near Tomioka Town (within the 20 km of the FDNPS) reported absorbed dose rates ranging from 1 to 5 μGy/h in 2017[15]. Our previous handheld measurements showed the median dose rate was 2.3 μSv/h in the difficult-to-return zone of Tomioka Town in 2017[16].

The dose rates in the Decontaminated area decreased faster than those in the Radioactive waste storage area and Non-decontaminated area from July 2018 to July 2019. Significant differences in ambient dose rates were observed among surveys in the Decontaminated area, Radioactive waste storage area and Non-decontaminated area ($p < 0.001$). Noticeable fluctuations in dose rates in the Radioactive waste storage area and Non-decontaminated area were observed. Also, a relatively stable downward trend was observed in the Decontaminated area.

The main reason for the decrease in dose rates over this 1-year period in Yonomori District is the decontamination efforts which have focused on removing deposits from roofs, decks and gutters; wiping off roofs and walls; high-pressure washing of houses and buildings; mowing lawns; removing fallen leaves and stripping topsoil in gardens; removing deposits in ditches and high-pressure washing of roads[10,17,18] (Supplementary Fig. S1). In our previous report, the effectiveness of removing topsoil for decontamination, and the positive relationship between soil radioactivity and air dose rates have been reported previously[16]. One report suggested that the total ^{137}Cs content in soils was 1200 Bq/kg on average (value range: 20–4400 Bq/kg), which was an 80% decrease from the values determined before the decontamination within agricultural fields in Tomioka Town[19]. The Ministry of the Environment, Japan reported that due to decontamination, the ambient rate 1 m above the ground surface was reduced by 60% in residential areas, and 42% on the roads[20]. Another report suggested that the average dose rate in the Decontaminated area was about 20% lower than that in the Non-decontaminated area[21]. Our study also showed that the dose decreased by 71.9% within 1 year of decontamination efforts in areas where the initial dose rate was 1.0 μSv/h (median) in the Decontaminated area (Yonomori District). In the present study, the small range and high frequency of sampling points with the Radi-probe system could concretely estimate the effects of decontamination.

Moreover, the physical decay of the ambient dose rates was calculated using dose conversion coefficients under the assumption that the depth profile of radiocesium did not change with time and the initial radioactivity of ^{134}Cs and ^{137}Cs were 9.0 and 8.8 PBq, respectively[1,22]. In the present study, the physical decay of radiocesium was estimated to be 7.5% from July 2018 to July 2019 (Supplementary Table S1). The reduction rates during research period in the Radioactive waste storage area and Non-decontaminated area were 21.1% and 27.9%, respectively. Our results showed that the reduction rates of radiocesium in all three districts were noticeably faster than its physical decay.

In Yonomori District, the decreasing time trends of the confidence levels of radiocesium were consistent with the decreasing time trends of the ambient dose rates. Furthermore, the distribution of ^{137}Cs in the Non-decontaminated area remained at a high level (Fig. 3). The confidence level of ^{137}Cs in the Non-decontaminated area, which is mainly covered by forest, showed a relatively slower decreasing trend compared with other areas. Previous studies also reported a longer ecological half-life in forested areas and suggested that the accumulation of radiocesium in association with the self-decontamination processes of forest canopies affects the temporal evolution of the ambient dose rate at the forest floor[23–26].

Previous studies indicated that the dose rates decreased due to radioactive decay, natural weathering effects, penetration of radiocesium into the ground, land use and decontamination[15,27–29]. The forest ecosystem also retains radionuclides; decreases in dose rates are typically slower than those in urban areas and annual doses can be very high[23,30–32]. Some studies have suggested that the rate of the decrease in radiocesium doses in Fukushima was faster than that in the forests contaminated by the Chernobyl nuclear accident[33]. Furthermore, Kato *et al*. reported that the rate of the decrease in radiocesium doses in mixed broad-leaved forests and deciduous broad-leaved forests during 2011–2016 was approximately 20% higher than the physical decay rate of radiocesium, which corroborates our findings (20.4%)[24].

In the Radioactive waste storage area, the ambient dose rates were sometimes higher in later surveys than in the first survey, which might result from radiocesium being resuspended in the air with dust particles due to dump truck traffic performing decontamination work and/or meteorological events[34,35]. The decreasing proportion of ambient dose rates in the Radioactive waste storage area suggested that human activities such as a contaminant waste storage project may lead to a 0–10% fluctuation in ambient dose rates (Table 1).

In the present study, the estimated annual effective dose of decontamination workers, as well as the residents of decontaminated areas, was lower than the annual effective dose limits recommended by the Japanese government[36]. Nevertheless, radiation safety education for workers is needed to appropriately protect them from radiation.

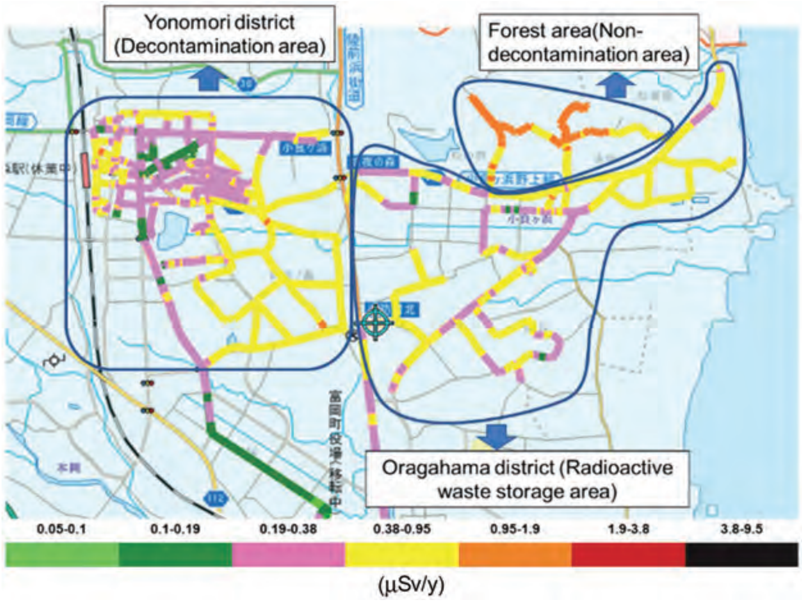

Figure 4. Real-time map of color-scaled ambient dose rates in the Difficult-to-return zone in Tomioka Town (May 2019). This map was modified by using PowerPoint software, from the map obtained by the car-borne survey using the Radi-probe system made in May 2019 (GIS software: Shobunsha Publications, Inc., Tokyo, Japan. https://www.mapple.co.jp/en/. The Radi-probe system: Chiyoda Technology Corp., Tokyo, Japan. http://www.c-technol.co.jp/eng). Blue lines show the three districts (Yonomori District: Decontaminated area; Oragahama District: Radioactive waste storage area, and Forested area: Non-decontaminated area). Reprinted from the map software for the Radi-probe system under a CC BY license, with permission (No. 61-G-081) from Shobunsha Publications, Inc., Tokyo, Japan; original copyright 2017 and Chiyoda Technology Corp., Tokyo, Japan.

We could not carry out all of the car surveys on the same routes because the Decontaminated area was expanding with progression of the decontamination efforts and some roads were temporarily blocked during the decontamination work. Furthermore, the dose rate transition with the season and weather was difficult to identify through horizontal comparison over 11 surveys. However, the main artificial radionuclides, such as ^{137}Cs, derived from the FDNPS accident could be analyzed to sufficiently low levels using the Radi-probe system. Moreover, the long-term follow-up monitoring in combination with various analytical apparatus and system such as car-borne survey and nuclides analysis of the environmental samples could be accurately evaluate the decontamination effects, external and internal radiation levels. These monitoring is extremely important for the reconstruction of affected areas around the FDNPS.

Materials and Methods

Survey location. The FDNPS (37°25′ N, 141°02' E) is located on the east coast of Honshu Island, approximately 200 km northeast of Tokyo. Tomioka Town (public office: 37°20' N, 141°0' E) is located 8.5 km south of the FDNPS. In the present study, we measured ambient dose rates and artificial radionuclides (mainly radiocesium) derived from the FDNPS accident in the difficult-to-return zone of Tomioka Town from July 2018 to July 2019 (Fig. 4).

The different-to-return zone of Tomioka Town was divided by the main road between Yonomori District and Oragahama District, both of which are located within 10 km of the FDNPS (Fig. 3). Yonomori District was designated by the government as a reconstruction and revitalization area and main decontamination efforts started in July 2018[37]. The decontamination work involved cleaning paved surfaces and roadsides and street drains, topsoil removal, weeding and pruning trees, washing building surfaces and demolish building[17,38]. Part of Oragahama District was designated a radioactive waste storage area and was decontaminated in 2014; however, the forested area of this district has not been decontaminated since the accident. In the present study, Yonomori District is referred to as the Decontaminated area, the radioactive waste storage area in Oragahama District is referred to as the Radioactive waste storage area, and the forested area of Oragahama District is referred to as the Non-decontaminated area.

Survey of ambient rates and radionuclides. We regularly measured the ambient dose rate from July 2018 to July 2019 (10 times in the Decontaminated area; 11 times in the Radioactive waste storage area; nine times in the Non-decontaminated area). The difficult-to-return zone of Tomioka Town was surveyed using a car-borne survey system, Radi-probe (Chiyoda Technology Corp., Tokyo, Japan. The handheld radiation detector model: HDS-101GN, Mirion Technologies, Inc., Japan)[6,39]. The Radi-probe system was installed in a vehicle and the meter's detector was set on the front passenger seat about 1 m above the ground. The ambient dose rates were measured and position coordinates and a photo were automatically taken every 5 seconds in addition to spectrum segments every 0.2 seconds. Gamma detection was performed by a large Thallium doped Cesium Iodide scintillator with high sensitivity (Typical 1400 cps per μSv/h for ^{137}Cs source). The measurable energy range of gamma-ray energy was 30 keV to 6 MeV, using a multichannel analyzer with 512 channels. Real-time maps with color-scaled ambient dose rates and gamma-ray energy spectra can be output. The detected energy peaks of radiocesium (^{134}Cs and ^{137}Cs) registered in the nuclear library (i.e., detected net count values) and their associated confidence intervals were obtained for the region of interest (with levels 1–10 used as reference values)[7,39].

Generally, the car chassis and wall acted as a shield to radiation from outside. The shielding factors were estimated by taking measurements inside and outside the car in open and flat areas at a high of 1 m above the ground. Since many factors such as the type of car and the number of passengers could influence the shielding factors[40], we calculated the shielding effects before each vehicle survey and the shielding factors were found to range from 1.1 to 1.6. For all surveys, vehicles were driven by the same person at a steady speed. The number of measurement points fluctuated due to restricted access to roads as decontamination efforts progressed. Combined with the output photos, the three districts were precisely divided. The measurement points ranged from 748 to 1408, 510 to 849 and 127 to 189 in the Decontaminated area, Radioactive waste storage area and Non-decontaminated area, respectively.

Effective dose. Effective doses were determined for external exposure based on the following formula:

$$E_i = (\mathrm{D}_{\mathrm{out}} - \mathrm{D}_{\mathrm{BG}}) \cdot \mathrm{T} \cdot \mathrm{R} \tag{1}$$

$$\mathrm{E}_{\mathrm{w}} = \sum_{i=1}^{12} E_i \tag{2}$$

$$\mathrm{E} = \mathrm{E}_{\mathrm{out}} + \mathrm{E}_{\mathrm{in}} \tag{3}$$

$$\mathrm{E}_{\mathrm{out/in}} = (\mathrm{D}_{\mathrm{out/in}} - \mathrm{D}_{\mathrm{BG}}) \cdot \mathrm{T} \cdot \mathrm{F} \cdot \mathrm{R} \tag{4}$$

$$\mathrm{D}_{\mathrm{in}} = r \cdot \mathrm{D}_{\mathrm{out}} \tag{5}$$

where E_i is the estimated external effective dose (mSv/month by median); E_w is the external effective dose for decontamination workers (mSv/y); E is the external effective dose for residents who are going to return to the Decontaminated area (mSv/y); $E_{out/in}$ is the external effective dose for outdoor and indoor workers; $D_{out/in}$ is the dose rate for a height of 1 m above ground outside and inside the house (μSv/h); D_{BG} is 0.04 μSv/h, which was measured in the area of interest before the accident[41]; T is the work time, 240 d × 8 h (normal labor standards in Japan); F is the occupancy factor[1]; R is the age-dependent dose conversion coefficient for adults (0.6)[22,42], and, *r* is the deposited gamma location factor for a wooden house (0.4)[43].

Statistical methods. All of the data were not normally distributed. The Mann-Whitney U and Kruskal-Wallis H tests were used to compare differences among the three areas in the same period and the time-trend within the same district. Regression lines were used to calculate the reduction rate of the average ambient dose rates.

Received: 19 November 2019; Accepted: 26 May 2020;
Published online: 23 June 2020

References

1. UNSCEAR. Sources, effects and risks of ionizing radiation: United nations scientific committee on the effects of atomic radiation 2013 report. I, (2013).
2. Fukushima Prefecture. Fukushima revitalization station. (Accessed August 23, 2019), http://www.pref.fukushima.lg.jp/site/portal-english/list385.html (Accessed July 31, 2019).
3. Nuclear Regulation Authority, Japan. Monitoring information of environmental radioactivity level. (Accessed Auguest 23, 2019), https://radioactivity.nsr.go.jp/en/ (Accessed July 31, 2019).
4. Ramzaev, V. *et al*. A backpack γ-spectrometer for measurements of ambient dose equivalent rate, H˙*(10), from 137Cs and from naturally occurring radiation: The importance of operator related attenuation. *Radiat. Meas.* **107**, 14–22 (2017).
5. Cresswell, A. J. *et al*. Demonstration of lightweight gamma spectrometry systems in urban environments. *J. Environ. Radioact.* **124**, 22–28 (2013).
6. Kobayashi, S. *et al*. Radioactive contamination mapping of northeastern and eastern Japan by a car-borne survey system, Radi-Probe. *J. Environ. Radioact.* **139**, 281–293 (2015).
7. Varley, A. *et al*. Reconstructing the deposition environment and long-term fate of Chernobyl 137Cs at the floodplain scale through mobile gamma spectrometry. *Environ. Pollut.* **240**, 191–199 (2018).
8. Sanada, Y., Urabe, Y., Sasaki, M., Ochi, K. & Torii, T. Evaluation of ecological half-life of dose rate based on airborne radiation monitoring following the Fukushima Dai-ichi nuclear power plant accident. *J. Environ. Radioact.* **192**, 417–425 (2018).
9. Sanada, Y., Orita, T. & Torii, T. Temporal variation of dose rate distribution around the Fukushima Daiichi nuclear power station using unmanned helicopter. *Appl. Radiat. Isot.* **118**, 308–316 (2016).
10. Ministry of the Environment of Japan. Environmental remediation in affected areas in Japan. (Accessed August 23, 2019), http://josen.env.go.jp/en/pdf/environmental_remediation_1905.pdf (2019).
11. Tomioka town office. The reproduction plan in difficult-to-return zone of Tomioka town (in Japanese) (Accessed August 23, 2019), http://www.tomioka-town.jp/material/files/group/3/ (2017).
12. Tomioka Town Office. Tomioka radiation information summary site. https://tomioka-radiation.jp/, (Accessed August 23, 2019).
13. JAEA. Database for Radioactive Substance Monitoring Data. https://emdb.jaea.go.jp/emdb/en/, (Accessed August 23, 2019).

14. Nakama, S., Yoshimura, K., Fujiwara, K., Ishikawa, H. & Iijima, K. Temporal decrease in air dose rate in the sub-urban area affected by the Fukushima Dai-ichi Nuclear Power Plant accident during four years after decontamination works. *J. Environ. Radioact.* **208–209**, 106013 (2019).
15. Yamaguchi, M. *et al*. Changes of absorbed dose rate in air by car-borne survey in namie town, Fukushima prefecture after the Fukushima Daiichi nuclear power plant accident. *Radiat. Prot. Dosimetry* 1–4, https://doi.org/10.1093/rpd/ncz023 (2019).
16. Matsuo, M., Taira, Y., Orita, M., Yamada, Y. & Ide, J. Evaluation of environmental contamination and estimated radiation exposure dose rates among residents immediately after returning Home to Tomioka Town, Fukushima Prefecture. *Int. J. Environ. Res. Public Health* **16**, 1481 (2019).
17. Ministry of the Environment of Japan. Decontamination Guidelines. (2013).
18. Ministry of the Environment. Environmental Remediation in Japan (Accessed January 7, 2020), http://josen.env.go.jp/en/pdf/progressseet_progress_on_cleanup_efforts.pdf (2018).
19. Kurokawa, K., Nakao, A., Tsukada, H., Mampuku, Y. & Yanai, J. Exchangeability of 137Cs and K in soils of agricultural fields after decontamination in the eastern coastal area of Fukushima. *Soil Sci. Plant Nutr.* **65**, 401–408 (2019).
20. Ministry of the Environment of Japan. Decontamination projects for radioactive contamination discharged by Tokyo Electric Power Company Fukushima Daiichi Nuclear Power Station accident: Chapter 5: Effects, verification, and risk communication of decontamination. http://josen.env.go.jp/en/poli, http://josen.env.go.jp/en/policy_document/pdf/decontamination_projects_1902_05.pdf 290 (2019).
21. Saito, K. *et al*. Summary of temporal changes in air dose rates and radionuclide deposition densities in the 80 km zone over five years after the Fukushima Nuclear Power Plant accident. *J. Environ. Radioact*. 0–1, https://doi.org/10.1016/j.jenvrad.2018.12.020 (2019)
22. Saito, K. & Petoussi-Henss, N. Ambient dose equivalent conversion coefficients for radionuclides exponentially distributed in the ground. *J. Nucl. Sci. Technol.* **51**, 1274–1287 (2014).
23. Andoh, M. *et al*. Measurement of air dose rates over a wide area around the Fukushima Dai-ichi Nuclear Power Plant through a series of car-borne surveys. *J. Environ. Radioact.* **139**, 266–280 (2015).
24. Kato, H., Onda, Y. & Yamaguchi, T. Temporal changes of the ambient dose rate in the forest environments of Fukushima Prefecture following the Fukushima reactor accident. *J. Environ. Radioact.* **193–194**, 20–26 (2018).
25. Nishikiori, T. *et al*. 137Cs transfer from canopies onto forest floors at Mount Tsukuba in the four years following the Fukushima nuclear accident. *Sci. Total Environ.* **659**, 783–789 (2019).
26. Manaka, T. *et al*. Six-year trends in exchangeable radiocesium in Fukushima forest soils. *J. Environ. Radioact.* **203**, 84–92 (2019).
27. Mikami, S. *et al*. The air dose rate around the Fukushima Dai-ichi Nuclear Power Plant: Its spatial characteristics and temporal changes until December 2012. *J. Environ. Radioact.* **139**, 250–259 (2015).
28. Saito, K. Temporal change of environmental contamination conditions in five years after the Fukushima accident. *EPJ Web of Conferences* **153**, 4 (2017).
29. Nakanishi, T., Matsunaga, T., Koarashi, J. & Atarashi-Andoh, M. 137Cs vertical migration in a deciduous forest soil following the Fukushima Dai-ichi Nuclear Power Plant accident. *J. Environ. Radioact.* **128**, 9–14 (2014).
30. Teramage, M. T., Onda, Y., Kato, H. & Sun, X. Impact of forest thinning on the dynamics of litterfall derived 137Cs deposits in coniferous forest floor after Fukushima accident. *Chemosphere* **239**, 124777 (2020).
31. Burger, A. & Lichtscheidl, I. Stable and radioactive cesium: A review about distribution in the environment, uptake and translocation in plants, plant reactions and plants' potential for bioremediation. *Sci. Total Environ.* **618**, 1459–1485 (2018).
32. Orita, M., Fukushima, Y., Yamashita, S. & Takamura, N. The need for forest decontamination: For the recovery of fukushima. *Radiat. Prot. Dosimetry* **175**, 295–296 (2017).
33. Konoplev, A. *et al*. Natural attenuation of Fukushima-derived radiocesium in soils due to its vertical and lateral migration. *J. Environ. Radioact.* **186**, 23–33 (2018).
34. Akimoto, K. Annual and weekly cycles of radioactivity concentration observed in fukushima city. *Health Phys.* **108**, 32–38 (2015).
35. Hosoda, M. *et al*. Evaluations of inventory and activity concentration of radiocesium in soil at a residential house 3 years afterthe Fukushima Nuclear accident. *Radiat. Prot. Dosimetry*, https://doi.org/10.1093/rpd/ncz071(2019).
36. Ministry of health, labour and welfare, Japan. Guidelines on Prevention of Radiation Hazards for Workers Engaged in Decontamination Works, https://www.mhlw.go.jp/english/topics/2011eq/workers/ri/gn/gn_141118_a01.pdf (Accessed August 23, 2019).
37. Ministry of the Environment of Japan. The progress of decontamination in Tomioka town (in Japanese), https://tomioka-radiation.jp/josen.html (Accessed August 23, 2019). (2019).
38. Ministry of the Environment of Japan. Decontamination Projects for Radioactive Contamination Discharged by Tokyo Electric Power Company Fukushima Daiichi Nuclear Power Station Accident:Chapter 1: History and Overview of Decontamination Projects. (2019).
39. Taira, Y. *et al*. Eight years post-Fukushima: is forest decontamination still necessary? *J. Radiat. Res*. 1–3, https://doi.org/10.1093/jrr/rrz051 (2019).
40. Inoue, K. *et al*. Impact on ambient dose rate in metropolitan Tokyo from the Fukushima Daiichi Nuclear Power Plant accident. *J. Environ. Radioact.* **158–159**, 1–8 (2016).
41. Ministry of the Environment of Japan. Additional exposure doses after an accident (example of calculation).(Accessed August 23, 2019), https://www.env.go.jp/en/chemi/rhm/basic-info/1st/02-04-09.html (Accessed July 31, 2019) (2018).
42. Profes, E. *et al*. Nuclear power facilities such as disaster prevention measures consignment expenses (measurement of continuous air dose rate that simulated life action pattern) (in Japanese). (2017).
43. Ministry of the Environment of Japan. Shielding and reduction coefficient. (Accessed August 23, 2019), https://www.env.go.jp/en/chemi/rhm/basic-info/1st/02-04-08.html (Accessed July 31, 2019) (2018).

Acknowledgements
We would like to thank all the study participants and the staff of Tomioka Town for their cooperation. This work was supported by Research on the Health Effects of Radiation organized by the Ministry of the Environment, Japan and Japan China Sasakawa Medical Fellowship.

Author contributions
Conceived and designed the observations: N.T., Y.T.; performed the observations: L.C., Y.T., M.M., M.O. and Y.Y.; analyzed the data: L.C. and Y.T.; wrote the paper: L.C. and Y.T. All authors have approved the final version of the manuscript.

Competing interests
The authors declare no competing interests.

Additional information

Supplementary information is available for this paper at https://doi.org/10.1038/s41598-020-66726-y.

Correspondence and requests for materials should be addressed to Y.T.

www.nature.com/scientificreports

SCIENTIFIC REPORTS
natureresearch

OPEN

Radiocesium concentrations in wild boars captured within 20 km of the Fukushima Daiichi Nuclear Power Plant

Limeng Cui[1,2], Makiko Orita[1]✉, Yasuyuki Taira[1] & Noboru Takamura[1]

The Fukushima Daiichi Nuclear Power Plant (FDNPP) accident in 2011 released large amounts of artificial radioactive substances into the environment. In this study, we measured the concentration of radiocesium (^{134}Cs + ^{137}Cs) in 213 muscle samples from wild boars (*Sus scrofa*) captured in Tomioka town, which is located within 20 km of the FDNPP. The results showed that 210 (98.6%) muscle samples still exceeded the regulatory radiocesium limit (100 Bq/kg) for general foods. Radiocesium (^{134}Cs + ^{137}Cs) levels ranged from 87.1–8,120 Bq/kg fresh mass (FM), with a median concentration of 450 Bq/kg FM. The median committed effective dose was estimated to be 0.070–0.26 μSv/day for females and 0.062–0.30 μSv/day for males. The committed effective dose for one-time ingestion of wild boar meat could be considered extremely low for residents in Tomioka. The relatively high levels of radioactivity found in this study suggest that the high variability of food sources may have led to the large accumulation of radioactive substances. These results suggest that comprehensive long-term monitoring is needed to identify risk factors affecting recovery from a nuclear disaster.

The Fukushima Daiichi Nuclear Power Plant (FDNPP) accident that occurred in 2011 released large amounts of artificial radioactive substances into the environment, particularly cesium-137 (^{137}Cs; 8.8 PBq; half-life: 30.2 years), cesium-134 (^{134}Cs; 9.0 PBq; half-life: 2.1 years), and iodine-131 (^{131}I; 120.0 PBq; half-life: 8 days)[1]. The introduced radionuclides were deposited over a wide area of Fukushima Prefecture and accumulated in local food[2–4]. From April 2012, the Japanese government set the regulatory limit for radiocesium in general foods as 100 Bq/kg[5].

After the Chernobyl Nuclear Power Plant accident, researchers reported that game animals were contaminated with artificial radionuclides[6–8]. Among all such animals, wild boars showed an especially high radiocesium concentration[9,10]. Gulakov *et al.* measured wild boars captured in a 10–35-km zone from the Chernobyl Nuclear Power Plant in 2008, and found that the average concentration of ^{137}Cs in the muscle tissue of wild boars remained as high as 37,000 Bq/kg[11], even at 22 years after the accident.

Tomioka town (37° 20′43.6″N, 141°0′31″E) is located within 20 km of the FDNPP[12,13]. Immediately after the disaster, almost all residents of Tomioka town were forced to evacuate. The Tomioka town office led infrastructure recovery efforts and decontamination processes to remove radiocesium fallout from the town. On April 2017, the Japanese government lifted the evacuation order for Tomioka town, except for a difficult-to-return zone that comprised almost 15% of the total town area. Although the residential areas, farmland, and forests close to residential areas have been widely decontaminated, it has been reported that the forest area remains contaminated with radionuclides derived from the FDNPP, 8 years since the accident[12]. Highly contaminated wild boars were reported as a considerable issue that led residents to hesitate to return to their hometown. In fact, internal radiation exposure from food remains a matter of concern for the residents of Tomioka town[13], who wish to know the radioactive levels of wild boar, including the possibility of consuming wild boar in the future. Therefore, the aims of this study were to determine the levels of radiocesium contamination in wild boars found in Tomioka town, Fukushima Prefecture, and, since wild boar is a traditional ingredient in Japanese cuisine, to evaluate the internal radiation exposure risk of consuming wild boar meat.

[1]Department of Global Health, Medicine and Welfare, Atomic Bomb Disease Institute, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan. [2]Department of Radiation Protection, Beijing Research Center for Preventive Medicine, Beijing, China. ✉e-mail: orita@nagasaki-u.ac.jp

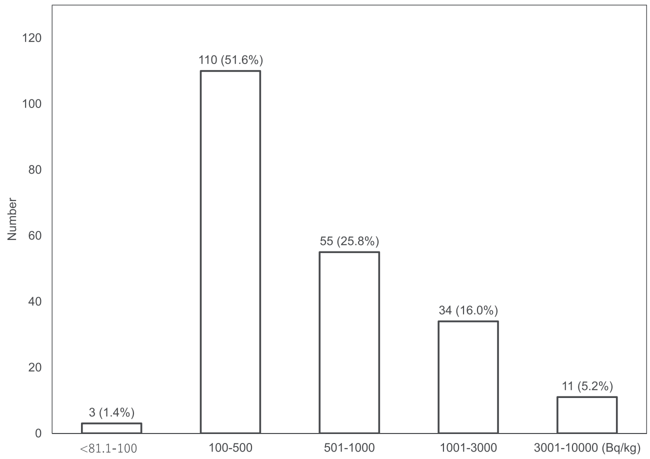

Figure 1. Distribution of radiocesium ($^{134}Cs + ^{137}Cs$) concentrations in the muscle tissue of wild boars from January to December 2019.

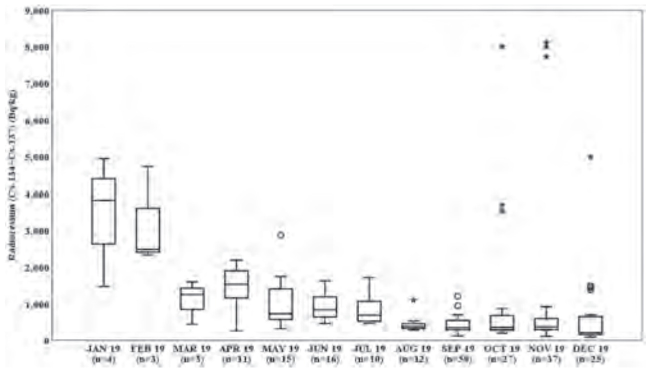

Figure 2. Time-dependency of radiocesium ($^{134}Cs + ^{137}Cs$) concentrations in the muscle tissue of wild boars. (Upper error bars: the largest data point excluding any outliers, Lower error bars: the lowest data point excluding any outliers, Open circles: outliers; Asterisks: extreme).

N = 213	Median (Minimum–Maximum)
Radiocesium (Bq/kg)	450 (87.1–8,120)
^{134}Cs (Bq/kg)	28.6 (n.d.*–509)
^{137}Cs (Bq/kg)	420 (81.1–7,610)

Table 1. Radionuclide concentrations (Bq/kg FM) in the muscle tissue of wild boars. *n.d.: could not be determined.

Results

Radioactivity concentration. Among the 213 wild boar (*Sus scrofa*) samples collected, 3 (1.4%), 110 (51.6%), 55 (25.8%), and 45 (21.2%) had radiocesium ($^{134}Cs + ^{137}Cs$) levels of <100, 100–500, 501–1,000, and $>1,000$ Bq/kg fresh mass (FM), respectively (Fig. 1). The minimum and maximum radiocesium concentrations were 87.1 Bq/kg FM and 8,120 Bq/kg FM, respectively, with a median concentration of 450 Bq/kg FM (Table 1). No significant correlation was found between radiocesium concentration and males and females (Mann–Whitney Test, $p = 0.516$) or between radiocesium concentration and the weight of the wild boars (Spearman correlation coefficient, $p = 0.376$). The average $^{134}Cs/^{137}Cs$ activity ratios in all samples were 0.08 in January 2019 and 0.06 in December 2019.

The distribution of radiocesium concentrations in the muscle tissue of wild boars for each month is shown in Fig. 2. Radioactivity concentrations varied significantly with month (Jonckheere–Terpstra test, $p < 0.05$).

Committed effective dose. Among 213 samples collected that contained radiocesium, the median committed effective dose ranged from 0.070 to 0.26 μSv for females and from 0.062 to 0.30 μSv for males, considering one-time ingestion of wild boar meat as the meat source (Table 2).

Age (y)	Female	Male
	Median (Minimum–Maximum)	Median (Minimum–Maximum)
1–6	0.069 (0.012–1.3)	0.072 (0.012–1.4)
7–14	0.18 (0.030–3.7)	0.19 (0.031–3.8)
15–19	0.26 (0.049–4.6)	0.30 (0.058–5.4)
20–29	0.17 (0.032–3.0)	0.18 (0.035–3.3)
30–39	0.15 (0.029–2.7)	0.21 (0.040–3.7)
40–49	0.16 (0.030–2.8)	0.24 (0.046–4.3)
50–59	0.12 (0.023–2.2)	0.18 (0.035–3.3)
60–69	0.070 (0.013–1.2)	0.12 (0.024–2.2)
å 70	NA*	0.062 (0.012–1.1)

Table 2. Committed effective doses for one-time ingestion of wild boar meat from Tomioka town (μSv/day). NA*: not available. Median pork consumption was 0 g among women aged >70 years in Japan in 2016.

Discussion

After the FDNPP accident, Nemoto *et al*. reported that the ^{137}Cs concentration of wild boar meat in Fukushima Prefecture from 2011 to 2016 was 900 ± 2,740 Bq/kg FM (mean ± standard deviation [SD]), with a maximum of 40,200 Bq/kg FM[14]. The Fukushima Prefecture government also published data on the radioactivity of wild boars that were captured in the Sousou area of Fukushima (1,737 km^2), and reported that the highest ^{134}Cs + ^{137}Cs concentrations from 2011 and 2019 were 5,720 in 2011, 61,000 in 2012, 20,000 in 2013, 30,000 in 2014, 30,000 in 2015, 3,100 in 2016, 14,000 in 2017, 460 in 2018 and 5000 Bq/kg in 2019, respectively[15]. Our results showed a mean ± SD radiocesium concentration of 866 ± 1,270 Bq/kg FM, with a maximum of 8,120 Bq/kg FM. Despite the ^{134}Cs/^{137}Cs activity ratios in this study agreed with those predicted from physical decay because the average ^{134}Cs/^{137}Cs activity ratios in all samples were 0.08 in January 2019 and 0.06 in December 2019, our results showed that the wild boar contamination level is still relatively high, even though 8–9 years had passed since the Fukushima accident.

Previous studies in Europe and Japan have reported that about 90% of the diet of wild boars consisted of plants, small animals, insects, and earthworms, based on the season and availability[16–20], and dietary habits are typically considered an important factor affecting radioactivity levels in wild boars[21,22]. At the same time, the ingestion of soil and deer truffles in winter has also been reported to be one of the causes of radioactive accumulation[8,21]. In 2019, the local government of Tomioka town published the results of an assessment of radiocesium concentrations in locally produced foods by a radioactivity monitoring center. The results showed that the maximum concentration of radiocesium was 99,700 Bq/kg FW in mushrooms, 4,600 Bq/kg FW in edible wild plants, 1,300 Bq/kg FW in chestnuts, 200 Bq/kg FW in persimmons, and 210 Bq/kg FW in bamboo shoots. The radiocesium concentrations in other food types, such as vegetables, potatoes, oranges, and plums, were mostly lower than 100 Bq/kg or not detected[23]. These findings suggest that mushrooms, edible wild plants, and soil with high radioactivity levels were the reasons for the high prevalence of contaminated wild boar in Tomioka town.

If the residents consume the wild boar meat as a meat source once, the median committed effective dose was in the range of 0.062 to 0.30 μSv/day, with a maximum value of 5.4 μSv/day. In Japan, the natural effective dose from food ingestion was estimated to be 99 μSv/y, which was 0.27 μSv/day[24]. Our results indicated that the median committed effective dose from consumption of wild boar meat was similar to or lower than the natural effective dose from food ingestion in Japan. Although, wild boar meat consumption was estimated based on pork consumption in Japan and wild boar meat consumption has been restricted since the FDNPP accident. Thus, the effective dose from the one-time ingestion of wild boar meat could be considered low for residents of Tomioka town.

This study did have some limitations. First, the sample size was small in the first few months of the study. Second, time trends and seasonal variations were still difficult to assess. Actually, seasonal change in radionuclide contamination in wild boar remains controversial[14,25]. Changes in food sources, eating habits, the natural environment, and human behavior may all affect radionuclide concentrations; therefore, continuous measurements are needed to determine how seasonal change affects the concentration of radiocesium in wild boars.

In conclusion, we showed that the wild boar contamination level is still relatively high, even though 8–9 years had passed since the Fukushima accident, but the effective dose from the one-time ingestion of its meat could be considered low for residents of Tomioka town. Long-term monitoring is needed in order to identify a long-term comprehensive risk evaluation such as internal exposure dose for recovery from the Fukushima nuclear disaster.

Methods

Sampling information. The Ministry of Agriculture, Forestry and Fisheries of Japan and Tomioka town office have established guidelines regarding the hunting of wild boars. Based on the Act on Special Measures for Prevention of Damage Related to Agriculture, Forestry and Fisheries Caused by Wildlife, Tomioka town office has asked licensed hunters to carry out the capture and processing of wild boars to prevent animal damage to agricultural and forestry products. The wild boars (*Sus scrofa*) were captured using box traps set by the local government and licensed hunters (Fig. 1). The licensed hunters have reported the hunting dates, hunting numbers, and information about the processed boar meat to the Tomioka town office every month. Prior to the study, we obtained approval from the Tomioka town office for use of pieces of legally obtained wild boar meat. In total, 213 pieces of wild boar meat were collected from January to December 2019 (males: 116, females: 97; weight range: 1.1–103 kg).

Samples of fresh wild boar meat (14–108 g) were minced and then enclosed in 100 mL plastic containers made of polypropylene for the radionuclide measurements. All samples were measured fresh and analyzed with a high-purity germanium detector (ORTEC, GMX30–70, ORTEC INTERNATIONAL Inc., Oak Ridge, TN, USA) coupled with a multi-channel analyzer (MCA7600, SEIKO EG&G Co., Ltd., Chiba, Japan). Integration times were 3,600 s for the wild boar samples. The measuring time was set to detect the objective radionuclide, and the gamma-ray peaks used for the measurements were 604.66 keV for ^{134}Cs and 661.64 keV for ^{137}Cs. Decay corrections were made based on the sampling date, and detector efficiency calibration was performed for different measurement geometries using mixed-activity standard volume sources (Japan Radioisotope Association, Tokyo, Japan). The relative efficiency was 31%, and energy resolution of the spectrometer was 1.85 keV for ^{60}Co. The correction factor of the sum-peak effect of ^{134}Cs and ^{137}Cs were almost 1, respectively. Activity concentrations of radiocesium were automatically adjusted based on the date of collection, and the data were defined as the activity concentrations at the collection date. The counting errors were $\pm$2.9 Bq/kg for ^{134}Cs (median) and $\pm$9.5 Bq/kg for ^{137}Cs (median), respectively. The ^{134}Cs concentrations in 7 samples were lower than the detection limits, which were in the range of 4.1–9.6 Bq/kg. Sample collection, processing, and analysis were executed in accordance with standard methods of radioactivity measurement authorized by the Ministry of Education, Culture, Sports, Science, and Technology, Japan.

Effective dose. The committed effective doses from the wild boar samples were estimated from the radioactive concentration of the fresh samples using Eq. (1):

$$H_{int} = C \cdot D_{int} \cdot \mathrm{e} \tag{1}$$

where C is the activity concentration of the detected artificial radiocesium (Bq/kg FM). Here, D_{int} represents the age-dependent dose conversion coefficients for ^{134}Cs (age 1 year, 1.6E-08 Sv/Bq; age 5 years, 1.3E-08 Sv/Bq; age 10 years 1.4E-08 Sv/Bq and age 15–70 years, 1.9E-08 Sv/Bq) and ^{137}Cs (age 1 year, 1.2E-08 Sv/Bq; age 5 years, 9.6E-09, age 10 years, 1.0E-08 Sv/Bq; and age 15–70 years, 1.3E-08 Sv/Bq) used in the assessments, which were provided by ICRP Publication 72[26], and e is quoted from the mean value of daily intake for age and sex. Because wild boar is not a conventional food in Japan, the government and research institutes have not published data on the amount of wild boar consumed. Consequently, wild boar meat consumption was estimated based on the median pork consumption in Japan published by the Ministry of Health, Labour, and Welfare in 2016 (males: 10–49.5 g/day; females: 0–42 g/day)[27].

Statistical methods. Data are expressed as medians, minimums, and maximums. Normality was checked using the Kolmogorov–Smirnov test. Because the variables were not normally distributed, non-parametric statistical tests were used. Differences in the concentrations of radiocesium in wild boars at each sampling month were evaluated using the Jonckheere–Terpstra test. Relationships between body weight and the radiocesium concentration in muscle tissue were evaluated using Spearman's rank correlation analysis. Differences in the concentrations of radiocesium between male and female wild boars were evaluated using the Mann–Whitney U test. P values < 0.05 were considered statistically significant. All statistical analyses were performed using SPSS Statistics 25.0 (IBM Corp., Armonk, NY, USA).

Data availability

All relevant data are within the paper.

Received: 3 March 2020; Accepted: 20 May 2020;
Published online: 09 June 2020

References

1. UNSCEAR. *Sources, effects and risks of ionizing radiation: United nations scientific committee on the effects of atomic radiation 2013 report* Volume I (2013).
2. Orita, M. *et al*. Radiocesium concentrations in wild mushrooms after the accident at the Fukushima Daiichi Nuclear Power Station: Follow-up study in Kawauchi village. *Sci. Rep.* **7**, 6744 (2017).
3. Tsuchiya, R. *et al*. Radiocesium contamination and estimated internal exposure doses in edible wild plants in Kawauchi Village following the Fukushima nuclear disaster. *PLoS ONE* **12**, e0189398 (2017).
4. Saito, R., Kabeya, M., Nemoto, Y. & Oomachi, H. Monitoring ^{137}Cs concentrations in bird species occupying different ecological niches; game birds and raptors in Fukushima Prefecture. *J. Environ. Radioact.* **197**, 67–73 (2019).
5. Ministry of Health, Labour and Welfare, Japan. Information on the Great East Japan Earthquake (Accessed 16 December, 2019). https://www.mhlw.go.jp/english/topics/2011eq/index_food.html (2019).
6. Marovic, G., Lokobauer, N. & Bauman, A. Risk estimation of radioactive contamination after the Chernobyl accident using bioindicators. *Health Phys.* **62**, 332–337 (1992).
7. Vilic, M., Barisic, D., Kraljevic, P. & Lulic, S. 137Cs concentration in meat of wild boars (Sus scrofa) in Croatia a decade and half after the Chernobyl accident. *J. Environ. Radioact.* **81**, 55–62 (2005).
8. Hohmann, U. & Huckschlag, D. Investigations on the radiocaesium contamination of wild boar (Sus scrofa) meat in Rhineland-Palatinate: A stomach content analysis. *Eur. J. Wildl. Res.* **51**, 263–270 (2005).
9. INTERNATIONAL ATOMIC ENERGY AGENCY. *Handbook of Parameter Values for the Prediction of Radionuclide Transfer in Terrestrial and Freshwater Environments. IAEA, Vienna*, **472** (2010).
10. Nakanishi, T. & Tanoi, K. (Eds) *Agricultural implications of the Fukushima nuclear accident The First Three Years. Springer, Tokyo* (Springer Open, 2016).
11. Gulakov, A. V. Accumulation and distribution of ^{137}Cs and ^{90}Sr in the body of the wild boar (Sus scrofa) found on the territory with radioactive contamination. *J. Environ. Radioact.* **127**, 171–175 (2014).
12. Taira, Y. *et al*. Eight years post-Fukushima: is forest decontamination still necessary? *J. Radiat. Res.* **60**, 705–707 (2019).

13. Matsunaga, H. *et al*. Intention to return to the town of Tomioka in residents 7 years after the accident at Fukushima Daiichi Nuclear Power Station: a cross-sectional study. *J. Radiat. Res.* **60**, 51–58 (2018).
14. Nemoto, Y., Saito, R. & Oomachi, H. Seasonal variation of Cesium-137 concentration in Asian black bear (Ursus thibetanus) and wild boar (Sus scrofa) in Fukushima Prefecture, Japan. *PLoS. ONE.* **13**, e0200797 (2018).
15. The official website of Fukushima Prefecture. Radiation monitoring survey results list (in Japanese) (Accessed 2 December, 2019). https://www.pref.fukushima.lg.jp/site/portal/wildlife-radiationmonitoring1.html (2019).
16. Cuevas, M. F., Ojeda, R. A., Dacar, M. A. & Jaksic, F. M. Seasonal variation in feeding habits and diet selection by wild boars in a semi-arid environment of Argentina. *Acta Theriol. (Warsz).* **58**, 63–72 (2013).
17. Rosvold, J. & Andersen, R. *Wild boar in Norway-is climate a limiting factor? NTNU Vitesnskapsmuseet Rapp* (2008).
18. Asahi, M. Stomach contents of wild boars (Sus scrofa leucomystax) in winter. *J. Mammal. Soc. Japan* **6**, 115–120 (1975).
19. Barrios-Garcia, M. N. & Ballari, S. A. Impact of wild boar (Sus scrofa) in its introduced and native range: A review. *Biol. Invasions.* **14**, 2283–2300 (2012).
20. Rosell, C., Herrero Cortés, J., Arias, P. & Couto, S. Preliminary data on the diet of wild boar living in a Mediterranean coastal wetland. *Galemys.* **16**, 115–123 (2004).
21. Semizhon, T., Putyrskaya, V., Zibold, G. & Klemt, E. Time-dependency of the ^{137}Cs contamination of wild boar from a region in Southern Germany in the years 1998 to 2008. *J. Environ. Radioact.* **100**, 988–992 (2009).
22. Ballari, S. A. & Barrios-García, M. N. A review of wild boar Sus scrofa diet and factors affecting food selection in native and introduced ranges. *Mamm. Rev.* **44**, 124–134 (2014).
23. The official website of Tomioka Town Office. Food of radioactive material inspection (Accessed 10 December, 2019). https://tomioka-radiation.jp/food/foods-hihakai.html (2019).
24. Ministry of the Environment, Japan. Comparison of exposure Doses per year. https://www.env.go.jp/en/chemi/rhm/basic-info/1st/02-05-03.html (2017).
25. Tagami, K., Howard, B. J. & Uchida, S. The time-dependent transfer factor of radiocesium from soil to game animals in Japan after the Fukushima Dai-ichi nuclear accident. *Environ. Sci. Technol.* **50**, 9424–9431 (2016).
26. ICRP. Age-dependent doses to the members of the public from intake of radionuclides—Part 5 compilation of ingestion and inhalation coefficients. *ICRP Publication 72.* (1996).
27. Ministry of Health, Labour and Welfare, Japan. Report on national health and Nutrition Survey (in Japanese) (Accessed 7 March, 2020). https://www.mhlw.go.jp/bunya/kenkou/kenkou_eiyou_chousa.html (2016).

Acknowledgements

We would like to thank all the study participants and the staff of Tomioka town office for their cooperation. This work was supported by the Fukushima Innovation Coast Promotion Project (Revitalization Knowledge Project) and a Japan China Sasakawa Medical Fellowship.

Author contributions

Conceived and designed the observations: N.T., M.O.; performed the observations: M.O., L.C. and Y.T.; analyzed the data: L.C. and M.O.; wrote the paper: L.C. and M.O. All authors have approved the final version of the manuscript.

Competing interests

The authors declare no competing interests.

Additional information

Correspondence and requests for materials should be addressed to M.O.

Reprints and permissions information is available at www.nature.com/reprints.

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

中华人民共和国驻长崎总领事馆

长崎发文[2020]010 号

感谢信

北京市疾病预防控制中心：

2020 年 4 月，停泊在长崎的意大利籍邮轮歌诗达大西洋号发生新冠肺炎聚集性感染事件，涉及 82 名中国籍船员。贵中心崔力萌同志热心参与我馆领保工作，主动投身海外抗疫斗争，利用自身专业知识和临床经验，通过微信与船员建立沟通渠道，及时开展心理咨询，介绍防控知识，为船员缓解焦虑情绪、保持乐观心态发挥了积极作用，用实际行动展现了“白衣天使”的时代风采。

谨向贵中心崔力萌同志表示衷心感谢。

中国驻长崎总领馆

2020 年 11 月 25 日

公益財団法人日中医学協会
TEL　03－5829－9123
FAX　03－3866－9080
〒101-0032 東京都千代田区岩本町 1-4-3
住泉ＫＭビル6階
URL：https://www.jpcnma.or.jp/