Yonsei–Nagoya University
Research Exchange Meeting on Health Sciences 2023

Program & Proceedings

November 10-11, 2023

Nagoya University
Nagoya Japan

Welcome Letter

Dear Professors and students of Yonsei and Nagoya Universities,

I am very pleased to invite you to the 2023 Yonsei-Nagoya University Research Exchange Meeting on Health Sciences. We are planning to hold our exchange meeting at Nagoya University this year. After the experience of COVID-19, hybrid holding techniques have become commonplace for us. Therefore, we decided to hold a hybrid meeting this year so that professors and students from Yonsei University could participate. We expect an active exchange between both universities again.

Sincerely,

Minoru Hoshiyama
Chairperson, School of Health Sciences, Nagoya University

Acknowledgement

November 11, Saturday

Yonsei-Nagoya University Research Exchange Meeting on Health Sciences 2023

Prenary session: Main Hall, East-Building, Daiko-campus, Nagoya University

10:00	Registration			
10:20	Opening Moderator	Prof. Kuniharu Imai	Nagoya	Prof. Kuniharu Imai
	Opening host remarks	Prof. Minoru Hoshiyama	Nagoya	School of Health Sciences, Nagoya University
	Guest remarks (Video message)	Prof. Eun Woo Nam	Yonsei	Dean of College of Software and Digital Healthcare Convergence, Yonsei University
10:40	Presentation of commemorative gifts			To College of Software and Digital Healthcare Convergence To Wonju College of Nursing
10:50	Information	Prof. Kuniharu Imai	Nagoya	
11:00	Group photo	All participants	Yonsei/Nagoya	

11:00-12:00	Paperwork	Sakura Science Students	Yonsei	
12:00-13:00	Lunch	Students	Yonsei/Nagoya	
12:00-13:00	Bissiness meeting on Lunch	Professors	Yonsei/Nagoya	
13:30～	Department sessions			

Nursing: Main hall（East building 4F）				
13:30	Opening remarks	Prof. Naoko Nishitani	Nagoya	
	Guest greetings	Prof. So-Mi Park	Yonsei	
13:45	Opening announcement	Natsuki Nakayama	Nagoya	
Session Ⅰ				
	Chair	Prof. Kazuteru Niinomi	Nagoya	Presentation 10minutes + Discussion 5minutes
13:50		Misao Kurita	Nagoya	Impact Of Gum Chewing In Daily LifeOn Autonomic Nervous System Activity
14:05		Chiyo Iwata	Nagoya	Impact of Gum Chewing on the Autonomic NervousSystem and Work Efficiency
14:20		Momoka Niihara	Nagoya	Early mobilization in patients undergoing laparotomy inJapan: A literature review
14:35		Jae Yeon Lee	Yonsei	Hospital infection control education programto improve nurses' infection control awareness andperformance: A literature review
14:50		Sounantha Phanthadala	Yonsei	Factors associated with exclusive breastfeeding: Aliterature review
15:05-15:30	Intermission			
Session II				
	Chair	Dr. Maki Tanaka	Nagoya	Presentation 10minutes + Discussion 5minutes
15:30		Mika Kawabata	Nagoya	Developing and testing the reliability and validity of asupport scale for family caregivers' appraisal
15:45		Ayako Nakayama	Nagoya	Factors Associated with Dementia Worry among Middle-Aged or Older Adults
16:00		Chinzaya Boldoo	Yonsei	Factors related to nurse turnover Intention: A literaturereview
16:15		Odbayar Delgerekh	Yonsei	Factors related to nurses' organizational commitment: Aliterature review
16:30		Woori Lee	Yonsei	Generations of Nurses in Korea: A Scoping Review
16:45	General comments Closing	Prof. Natsuki Nakayama		
16:55	Closing remarks	Prof. Midori Asano	Nagoya	

Impact Of Gum Chewing In Daily Life
On Autonomic Nervous System Activity

Misao Kurita[1], Natsuki Nakayama[1], Yuki Kuno[2],

Chiyo Iwata[1], Sota Okabe[1], Momoka Nihara[1], Yoshimi Moriwaki[1]

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Introduction

Among the various effects of mastication exercises, there have been many studies on the effects of chewing gum on humans. Several studies on changes in heart rate variability during gum chewing have been conducted; however, masticatory motor stimuli were controlled in the laboratory or by metronomes [1] [2]. Little is known about the influence of mastication on autonomic nervous activity in daily life. Therefore, this study aimed to investigate the influence of gum chewing on heart rate variability in daily life and to elucidate some aspects of the significance of the act of mastication.

Methods

The participants were undergraduate and graduate students aged 20 years or older. Exclusion criteria were people who had allergies to gum ingredients, ongoing dental treatment, and a history of temporomandibular joint problems.

They completed a questionnaire about their date of birth, sex, height, weight, gum chewing habits, and the reasons for chewing gum.

To capture autonomic nervous activity indices, we fitted each participant with a Holter electrocardiograph and began the recording. The participants were asked to rest in a sitting position for 5 min without doing anything and then to chew gum for 5 min. Then, recording with the Holter electrocardiograph was completed. To account for the differences in blood glucose levels during meals, the experiment was conducted at least 2 h after a meal.

The normal RR interval was extracted from ECG data. Frequency analysis was then performed using the Mem method, and low-frequency power [LF (range: 0.04–0.15 Hz)] and high-frequency power [HF (range: 0.15–0.4 Hz)] were obtained. The average heart rate (HR), HF, and LF/HF values were calculated for 5 min of rest and 5 min of gum chewing. HF indicates parasympathetic activity; LF/HF, sympathetic activity [3]. The Wilcoxon signed-rank test was used to evaluate the differences between autonomic nervous activity indices with and without gum chewing. Statistical significance was set at p < 0.05.

This study was approved by the Bioethics Review Committee of the Nagoya University Graduate School of Medicine (Approval no. 21-144-2).

Results

Nineteen men and women who agreed to participate in the study were analyzed (Table 1).

The HR at 5 min of rest was 77 (55–99) bpm, and that at 5 min of gum chewing was 74 (60–101) bpm. The HR during gum chewing was significantly lower than that during no gum chewing (P = 0.027). The HF during 5 min of gum chewing was 503 (35–1977) ms², while the HF during 5 min of rest was 1042 (57–9695) ms². Therefore, HF with gum chewing was not significantly different from that without gum chewing (P = 0.445). LF/HF at 5 min of rest was 3.7 (0.7–6.8), while LF/HF at 5 min of gum chewing was 2.9 (0.5–5.5). The LF/HF with gum chewing showed a significant decrease compared to the LF/HF without gum chewing (P = 0.036).

Discussion

In the present study, 5 min of gum chewing did not significantly change the HF but significantly decreased the LF/HF. This suggests that gum chewing does not have an impact on HF but suppresses sympathetic activity and consequently increases parasympathetic activity.

A previous study reported that the alpha wave activity increased after gum chewing, which brought about relaxation [4] [5] [6]. In the present study, inhibition of sympathetic nerve activity by gum chewing was observed, which may have resulted in a relaxing effect.

However, a previous study reported an increase in sympathetic nerve activity after 6 min of gum chewing [1]. In the present study, the HR was significantly decreased by gum chewing, and sympathetic nerve activity was

suppressed. In the previous study, the experiment was conducted after lunch, whereas in this study, the experiment was conducted more than 2 h after the meal. Therefore, it is likely that HR did not undergo a postprandial compensatory mechanism that affected the increase in HR [7] in this study.

One limitation of this study is that the participants were limited to healthy young men and women. Therefore, to generalize the results of this study, it is necessary to examine the results for people of various ages and sociodemographic characteristics. In addition, because the duration of gum chewing in this study was only 5 min, the effects of longer chewing on autonomic nervous system activity should be investigated in the future.

Conclusion

Gum chewing for 5 min did not change parasympathetic nerve activity but decreased HR and suppressed sympathetic nerve activity. Gum chewing for 5 min in daily life is expected to have a relaxing effect by suppressing sympathetic nerve activity.

Table 1: Summary of participant data

		n	(%)	median	(range)
age				21	(21 – 22)
sex	man	6	(31.6)		
height				160	(146 - 182)
weight				50	(44 - 69)
frequency of gum chewing	everyday	0	(0)		
	about 3 days per week	2	(10.5)		
	about 1 day per week	2	(10.5)		
	about 1 day per month	3	(15.8)		
	little	12	(63.2)		
shape of gum	granular	18	(94.7)		
	plate	1	(5.3)		
time to chew a piece of gum				25	(5 - 60)
taste of gum	mint	12	(63.2)		
	Fruit	5	(26.3)		
	other	2	(10.5)		
reason for gum chewing	sleepy	5	(26.3)		
	given	2	(10.5)		
	clear one's mouth	4	(21.0)		
	study	3	(15.8)		
	concentration	1	(5.3)		
	hunger	3	(15.8)		
	class	1	(5.3)		

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Impact of Gum Chewing on the Autonomic Nervous System and Work Efficiency

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Introduction

Chewing gum affects both sympathetic and parasympathetic nerves [1]. In addition, chewing gum has been reported to reduce stress [2], increase short-term memory [3], and reduce subjective fatigue in computing tasks [4]. It has been shown that the effects of gum chewing on the sympathetic nervous system and the positive effects on calculation tasks are related [5,6]. However, whether the influence of gum chewing on the parasympathetic nervous system is related to its impact on task performance remains unclear. In addition, it is not clear how many minutes of gum chewing are required to achieve these effects, as the duration of gum chewing varies among the previous studies. Furthermore, calculation tasks incorporated as work tasks in many studies have been less representative of contemporary professional activities, where massive calculation tasks are less common. Therefore, in this study, we investigated the effects of chewing gum at various time points on autonomic nervous activity indicators and typing tasks in healthy adults.

Methods

Initially, the participants were equipped with a Holter monitor and completed a questionnaire regarding their age, sex, height, weight, and gum chewing habits. Measurements with gum chewing were performed using the following protocol: After 5 min of resting in a sitting position, the first typing session was conducted without gum chewing. After completing the first 5-minute typing session, participants began chewing gum and continued until the completion of the third typing session. Five minutes after the start of gum chewing, a second typing session was initiated and lasted 5 min. After typing was completed, participants remained seated in a resting state. Finally, the third typing session commenced 20 min after the initiation of gum chewing. After the third typing session, the Holter monitor was removed and the experiment was concluded. Measurements without gum chewing were performed using the same protocol as those with gum chewing, except for the gum chewing process.

We recorded the total number of types (counts) and rate of correct types (%) after each typing session. Participants were randomly divided into two groups, with half of them undergoing measurements without gum chewing, followed by a 20-minute break, and then measurements with gum chewing. The other half started with measurements with gum chewing, followed by measurements without gum chewing after a 20-minute break.

Results

Basic characteristics of participants

Eighteen participants (12 females and six males) from Nagoya University were included in the analysis. The participants were 21 (21-22) years old, 160.0 (146-182) cm tall, and had a BMI of 20.5 (17.1-27.2). Regarding gum chewing habits, more than a half of the participants (66.7%) answered that they rarely chew gum.

Parasympathetic nerve activity index (HF)

The HF during the first 5 min after the initiation of the third typing session with gum chewing was significantly higher than that during the first 5 min after the initiation of the first typing session before gum chewing (361 (32-1933) ms^2 vs. 341 (43-1718) ms^2, p = 0.044).

Total typing count

The typing count of the third typing session with gum chewing increased significantly compared with that of the first typing session before chewing gum (631 (461-906) times vs. 596 (439-932) times, p =0.006). Without chewing gum, the typing count was significantly higher in the second typing session than in the first (644 (476-933) times vs. 642 (458-935) times, p =0.027).

Correct typing count

The correct typing count of the third typing session with gum chewing was significantly higher than that of the first typing session before gum chewing (576 (429-813) times vs. 535 (406-846) times, p =0.013).

Discussion

Parasympathetic nerve activity index (HF)

A study by Hashizume et al. suggested that chewing gum for 5 min leads to greater stress reduction within 10 min after chewing gum compared to drinking water or simply having gum in the mouth without chewing [7]. Additionally, Ishiyama et al. reported that 6 min of gum chewing led to sympathetic nervous system activation during gum chewing and parasympathetic nervous system activation after gum chewing [1]. These studies have shown that the parasympathetic nerve activity is activated after at least 5 min of chewing gum, resulting in a relaxing effect. In the present study, based on HF fluctuations, it was considered that during the third typing session, 20 min after the start of gum chewing, the parasympathetic nervous system was still activated similarly to the state after gum chewing. Therefore, it is hypothesized that 20 min of gum chewing increases HF and induces relaxation compared to not chewing gum.

  Total typing count and correct typing count
Sasaki et al. showed that the work output decreased in calculation tasks because of the distraction of having something in the mouth [4]. In the present study, the total typing count did not increase significantly after 5 min of gum chewing, suggesting that 5 min of gum chewing may not affect work efficiency.

Hirano et al. suggested that chewing enhances concentration during chewing and promotes the processing of working memory [8]. Fantozzi et al. reported that chewing gum for 2 minutes increased the speed of extracting specific numbers from a sequence, both immediately after and 30 minutes after chewing [9]. Furthermore, Tojo et al. found that calculation task performance during gum chewing tended to be higher in a group that chewed gum than in a group that did not, although the difference was not significant [6]. Ishiyama et al. showed that 6 min of gum chewing activated sympathetic nerve activity during gum chewing and parasympathetic nerve activity after the end of gum chewing [1]. The improvement in concentration and working memory processing during chewing shown by Hirano et al. and the improvement in performance on a calculation task shown by Tojo et al. are considered to be associated with the activation of sympathetic nerves. In our study, HF increased after 20 min of gum chewing but did not increase after 5 min of gum chewing. In addition, both total and correct typing counts increased after 20 min of chewing; they did not increase after 5 min of gum chewing. This suggests that chewing gum for 20 minutes is effective in increasing work efficiency and is associated with an increase in HF. In conclusion, gum chewing for 5 min does not affect work efficiency; however, gum chewing for 20 min is expected to activate the parasympathetic nervous system and enhance work efficiency.

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Early mobilization in patients undergoing laparotomy in Japan: A literature review

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Introduction

Early mobilization after laparotomy is considered effective in preventing postoperative complications, promoting wound healing, and reducing the length of hospital stay [1][2]. In Japan, emphasis on the importance of early mobilization as an integral part of acute rehabilitation for post-laparotomy patients is needed to reduce medical costs.

Nursing interventions play a crucial role in facilitating the early mobilization of patients undergoing open laparotomy. Nonetheless, Nakanishi et al. have shown that postoperative early mobilization methods vary based on the nurses' years of experience [3]. Moreover, Sato et al. reported cases wherein early mobilization for patients undergoing laparotomy did not proceed as intended. The patients expressed concerns such as, "Is it safe to move so soon after surgery?" and the nurses expressed assumptions and subjective judgments such as, "The patient is in pain, so he will not be able to move" [4]. Hanamura et al. found that postoperative pain is exacerbated by the strain exerted on the abdominal muscles when transitioning from the supine to sitting positions [5]. This finding suggests that early mobilization after laparotomy is particularly difficult because of wound pain. However, no studies in Japan have identified the interventions for early mobilization after laparotomy.

This study aimed to identify effective strategies for promoting early mobilization in patients undergoing open laparotomy in Japan through a literature review.

Methods

The literature search was conducted using the Central Medical Journal (Ichu-shi Web), which covers all nursing literature in Japan. We searched for original articles published between 2015 and 2020, using the research keywords "early mobilization" and "laparotomy," which yielded 18 articles. The studies excluded were those that did not discuss postoperative mobilization, whose target operation was not laparotomy, that described the biological effects of early mobilization, and that discussed inhibitors for early mobilization. Seven articles were included in this analysis.

Results

There were two articles on the effects of preoperative care on postoperative early mobilization. They included "family orientation" and "preoperative rehabilitation."

There were four articles on nursing care and focus points for getting out of bed.

There was one article on the effects of perioperative rehabilitation.

Discussion

1. Standardized perioperative protocols

Of the seven articles examined, most focused on the preoperative interventions by the medical staff and postoperative care provided by the nurses. Only one article discussed standardized perioperative protocols, and those were for cancer patients. These results suggest that comprehensive perioperative protocols are yet to be established for all surgical patients in Japan. Hori et al. reported that although the contents and methods of the interventions varied previously, the introduction of perioperative rehabilitation helped establish a unified care system and the promotion of early mobilization. In the near future, validation of the effectiveness of perioperative protocol interventions would be necessary not only for cancer patients but also for other surgical patients.

Kato et al. compared an intervention group, receiving preoperative rehabilitation by other medical professionals and early mobilization immediately postoperatively, and a control group, which simply awaited postoperative spontaneous mobilization [6]. The results showed that compared to the control group, the intervention group showed earlier stabilization in water delivery balance, earlier normalization of the nitrogen balance, and earlier restoration of the total lymphocyte count. Additionally, the intervention group demonstrated inhibition of aspartate aminotransferase elevation. These results suggest that preoperative rehabilitation and early postoperative mobilization promote the postoperative recovery of metabolic functions.

2. Nurses' anxiety regarding the safety of early mobilization

Several articles reviewed in the literature described that nurses are anxious when assisting patients because the

ward nurses have to decide when to start and stop the early mobilization process [7]. This is an inhibitory factor for the nurses in proceeding with early mobilization. Instead of letting the ward nurses decide, we suggest establishing standard criteria for starting and stopping the early mobilization process. This will ensure safety and allow nurses to assist in weaning without any concerns.

The Japanese Society of Intensive Care Medicine (JSICM) has formulated the "initiation criteria for early mobilization and early active exercise" and "cancellation criteria for early mobilization and early active exercise" in the intensive care unit (ICU) [8]. Sato et al. reported the initial weaning of ICU patients following these criteria and evaluated their pain levels and vital signs [4]. Most patients who were unable to meet the discontinuation criteria or discontinued early mobilization showed worsened vital signs. These findings suggest that the implementation of specific criteria can effectively enhance the safety of early mobilization.

The discontinuation criteria for early mobilization proposed by the JSICM targeted ICU patients and did not apply to the hospital ward patients, where the ward nurses have to make these decisions. Few studies have validated the safety of early mobilization in hospital ward settings based on the JSICM criteria. Therefore, proposing the initiation and discontinuation criteria for early mobilization in ICUs as well as hospital wards is warranted while assessing the safety of these criteria.

Conclusion

We reviewed the literature to identify effective strategies for early mobilization in patients undergoing open laparotomy; however, no specific interventions were identified. In the future, the development of perioperative protocols is warranted based on the biological responses to ensure the safety of early mobilization. Specifically, we should implement interventions with standardized timing and content from the preoperative period and establish postoperative criteria for initiation and discontinuation.

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Hospital infection control education program to improve nurses' infection control awareness and performance: A literature review

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Introduction

Nurses have high frequency of direct contact with patients and play critical role in hospital infection spread prevention and control. It has been confirmed that the more nurses have high infection control awareness, the better they perform infection control [1, 2]. Nurses' infection control performances according to infection control education and instruction not only reduces the risk of infection among nurses but also provides patients a safer hospital environment and has become an important factor to block infection spread [3].

The importance of hospital infection control education program to improve a nurse's infection control awareness and performance has been magnified [4]. However, there is a lack of basic data and evidences about hospital infection control program's characteristics and effect for improvement of infection control awareness and performance. The purposes of this study was to 1) identify the nurses' infection control awareness and performance of hospital infection control education programs and 2) identify the characteristics and effects of hospital infection control education programs to improve awareness and performance through a literature review.

Methods
1) Search Strategy

This literature review was searched from August to September 10, 2023, through two electronic databases: MEDLINE (via PubMed) and RISS. The search was not limited to language, literature type, or study design. The search strategy terms included the following concepts: (1) 'Nurse' for population, (2) 'Infection control,' and 'Infection education program' for intervention, (3) 'Awareness,' and 'Performance' for outcome, and (4) 'Hospital' for setting.

2) Eligibility Criteria

Inclusion criteria were as follows: 1) studies that enrolled nurses working in hospitals as participants; 2) studies published in all languages; and 3) studies published between 2013 and 2023. Exclusion criteria were as follows: 1) studies that did not use a quantitative design; and 2) studies that did not report the study methods.

Results
1) Search Results

The search strategy identified 895 articles. A total of 24 article titles and abstracts were reviewed. The full texts of the 10 articles were reviewed for eligibility. Finally, five studies were included in the review.

2) Characteristics of Selected Studies and Participants

The characteristics of five studies finally selected were identified according to country, research design, setting, purposes, measures and outcomes. The three studies [5-7] targeted nurses at inpatient ward and the two studies [8, 9] targeted nurses at intensive care units (ICU). The two studies were cross sectional [5, 7], one was a systematic review [6], and two were quasi-experimental studies [8, 9].

3) Nurses' Infection Control Awareness and Performance of Infection Control Education Programs

According to the result of the one systematic review study [6] and two cross-sectional studies [5, 7], Hammoud et al. [5] identified that scores of infection control awareness and standard prevention were at an appropriate level but performance of healthcare associated infections and hand hygiene were not proper. Alrubaie et al. [7] identified the nurses' knowledge and performance of infection control of 100 nurses who directly contact patients in two private hospitals in S-city of Yemen. The result showed that the nurses' infection control knowledge and performance were at a high level. Nasiri et al. [6] analyzed 18 studies to survey nurses' knowledge, performance, and attitude of infection control and standard prevention. As a result, it has been identified that nurses had appropriate knowledge and positive attitudes about healthcare association infections but their infection control performances were not good.

4) Effects of Infection Control Education Program

According to the result of the two quasi-experimental studies [8, 9], Lim [8] provided education for multidrug-resistant bacterial infection control 3 times for 30 minutes each course for 4 months targeting 65 nurses who were working in a neonatal ICU in a university hospital in Korea, by using videos and educational materials. As a results, not only knowledge but also hand hygiene performance were improved. Specially, the rate of multidrug-resistant bacteria infection was reduced.

Galal et al. [9] provided infection control education for 1 month targeting 125 nurses who working in pediatric ICU of a university hospital in Egypt by using presentation about infection control principle and instruction, and video showing proper hand hygiene. As a results, nurses' knowledge and attitude improved after taking infection control program education.

Discussion

According to the two cross sectional studies [5, 7] and one systematic review [6], it has been revealed that nurses' infection control knowledge level was high but their infection control performance was inefficient. In addition, it has been confirmed that satisfactory knowledge improvement resulted through infection control education. However, there is still the demand for additional hospital infection control education programs to improve performance.

According to the two intervention studies [8, 9], nurses' infection control awareness [8, 9] and performance [8] were meaningfully improved through infection control education programs. It has been confirmed that nurses' infection control performance ability could also be improved by improving nurses' infection control awareness through effective infection control education [8]. However, Galal [9] did not check an infection control performance through an infection control education program. Further studies are needed to confirm the effectiveness of infection control education programs through additional searches through database expansion. Also, additional intervention studies are needed to confirm the infection control performance.

Even though the demand for hospital infection control education targeting nurses has been increased, intervention studies have been insufficient. In addition, due to the lack of verification of the effectiveness of hospital infection control education in terms of performance, following up efforts to evaluate and improve the infection control education program's effectiveness are required. This study recommends effective and various educational methods applied hospital infection control education programs must be developed for nurses' improvement in infection control awareness and performance.

Conclusion

This literature review identified that nurses' infection control awareness was high but infection control performance was insufficient. This study was also confirmed that awareness and performance were increased through infection control education, but there are still difficulties in identifying reasonable effects in terms of performance. An infection control education program needs to be developed to improve nurses' infection control awareness and performance, as nurses are critical medical workforces to prevent and control infection spread within a hospital.

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Factors associated with exclusive breastfeeding: A literature review

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Background

Exclusive breastfeeding provides immune protection for infants and supports their growth and development [1]. It also reduces the risk of respiratory and gastrointestinal infections, ultimately leading to lower mortality rates compared to infant formula feeding. Globally, the rate of exclusive breastfeeding, as measured by a 24-hour diet recall, increased from 24.9% in 1993 to 35.7% in 2013 [2]. Numerous studies have explored the factors that influence exclusive breastfeeding. Therefore, the authors systematically reviewed potential factors associated with exclusive breastfeeding, based on the results of previously published research articles. This literature review aims to enhance understanding of exclusive breastfeeding practices and promote more effective encouragement of exclusive breastfeeding in Laos.

Objective

This study aimed to identify the factors associated with exclusive breastfeeding in mothers of infants.

Methods

The databases PubMed, Embase, CINAHL, and Cochrane Library were searched using the key words "exclusive breastfeeding" and 'woman." Descriptive studies published between 2013 and 2023 in English were reviewed. In total, 751 references were identified by searching, but only 7 studies met our inclusion criteria (Figure 1).

Figure 1. Flow chart of article selection.
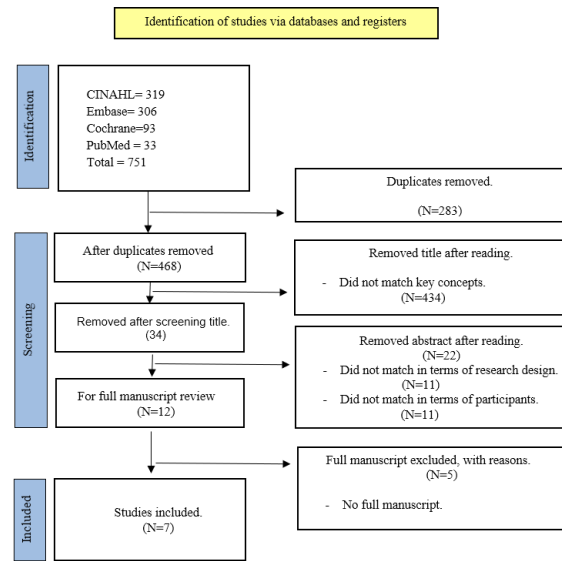
Results

1. Characteristics of selected articles

The publication years of the papers included in this review ranged from 2017 to 2022, and the studies were from 5 Asian countries and 1 African country. The subjects of the study were mothers with infants aged 6 to 24 months, and the number of participants varied from 80 to 3,541.

2. Identified associated factors

The variables that showed statistically significant associations with exclusive breastfeeding among mothers of infants included the mother's age at marriage, maternal motivation, marital status, occupation, breast complications, level of education, type of delivery, income, socioeconomic status, frequency of antenatal care visits, and wealth index.

3. Classification of associated factors based on the socio-ecological model

Intrapersonal factors with statistically significant associations with exclusive breastfeeding, as classified based on the socio-ecological model, were maternal age at marriage, maternal motivation, maternal status, mother occupation, type of birth, breast complication, mothers' education, and mothers with poor socioeconomic status. Region of residence was a significant community/society factor.

Conclusion

Most of the significant variables identified in this review were not maternal characteristics that could be changed through a nursing intervention (e.g., maternal age at marriage, mother's occupation, and mother's education). However, certain significant variables, such as maternal breastfeeding knowledge and motivation, as well as support from the husband, could potentially be modified through nursing interventions. Furthermore, the majority of these studies were conducted in developing countries in Asia and Africa.

This literature review demonstrates that to encourage exclusive breastfeeding among mothers of infants in Laos, it is crucial to offer tailored interventions. These interventions should target modifiable maternal factors in future studies, including information (knowledge), motivation (husband's support), and behavioral skills (self-efficacy), all of which are grounded in the IMB model.

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Developing and testing the reliability and validity of a support scale for family caregivers' appraisal

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Introduction

Family caregivers of care-dependent people are at high risk of experiencing psychological distress and depression [1]. At the same time, caregivers perceive a positive impact from their caregiving experiences [2]. In addition, positive appraisal of caregiving was associated with higher life satisfaction [3]. Previous research has clarified that the support of visiting nurses (e.g., collaborating with family caregivers in patient care) promotes positive appraisal of family caregivers and controls negative appraisal of caregiving (e.g., by alleviating associated burdens) [4,5]. Family caregivers identified healthcare professional advice as one of their significant needs [6]. However, few measures have examined support for family caregivers' appraisal. This study aimed to develop a support scale based on family caregivers' appraisal and examine its reliability and validity.

Methods

1. Item generation

The initial item pool was compiled in three steps:

The first steps: A questionnaire was developed based on previous studies describing the support that visiting nurses offer family caregivers' appraisal. The results showed that there were 37 items.

The second step: Interviews were conducted with visiting nurses, asking them about the support they provide to family caregivers' appraisal. The scale initially consisted of 42 items.

Third step: Three nurses and two researchers formed an expert panel. The panel examined 42 items individually, and similar items were grouped. Finally, 16 items were prepared.

2. Study Participants

The study participants were 87 family caregivers providing home-based care for a family member.

3. Data collection

Participants were selected from eight home-visit nursing stations located in various areas of Japan. The home care support offices agreed to our study after watching an online study presentation by researchers. Visiting nurses distributed the questionnaires to family caregivers.

The Ethics Committee of the Nagoya University Graduate School of Medicine approved the study (Approval no. 21-138-2)

4. Measures

Participants answered a self-administered questionnaire.

(1) Characteristics of the family caregiver and care recipient. (e.g., gender, age, duration of care, and relationship to the caregiver)

(2) The 16-item "a support scale for family caregivers' appraisal" The item scores (ranging from 0-3) that belonged to the domain were summed. Higher scores indicated recognition of support from the visiting nurse.

(3) To assess criterion-related validity, we compared the questionnaire against an existing scale for measuring caregiver coping strategies. The scale was developed by Okabayashi [7]. We selected one factor, "Formal Support Seeking" from among five caregiver coping strategies.

5. Statistical Analysis

To verify the validity of our scale, we conducted an exploratory factor analysis using the maximum-likelihood method and varimax rotation. Criterion-related validity was assessed by comparing the mean performance using Pearson correlation coefficients. Confirmatory factor analysis was conducted to determine the validity of the factor structure. In the reliability testing, Cronbach's alpha coefficients were confirmed. Descriptive statistical analyses were performed using SPSS Version 28 and Amos Version 29 software.

Results

1. Caregiver and Care Recipient Characteristics

The mean age and SD of caregivers was 68.4±11.9 years; 30 (34.5%) were male, and 57 (65.5%) were female. The mean age and SD of the care recipients were 80.8 ± 12.6 years. Most caregivers, 57 (69.5%), had less than five years of caregiving experience.

2. Validity Analysis

The original 16 items were examined. Item 15 was omitted as it subsumed multiple factors. In addition, its factor loading exceeded 0.3. The item content of the factors identified three subscales, "empathy and collaboration in caregiving" (*Factor 1*), "support that considers the caregiver's and family's wishes" (*Factor 2*), and "provision of information and skills regarding the recipient's care" (*Factor 3*). (Table 1)

The caregiver coping strategies scale (*Formal Support Seeking*) was used to examine criterion-related validity. It produced correlation coefficients (*r*) of 0.354–0.477. Moreover, the confirmatory factor analysis of this model was represented by GFI＝0.807, AGFI＝0.734, CFI＝0.807, and RMSEA＝0.095.(Figure1)

3. Reliability Analysis

The Cronbach's alpha coefficient for the entire scale was 0.914. (Table1) The I-T correlations between the items and the factor scores showed correlation coefficients of 0.5 or higher for all items and factors.

Discussion

The scale developed in this study was reliable and valid. The support scale for family caregivers' appraisal can help identify how much support they received as viewed from their perspective. Continuous implementation of this scale is required based on the duration of caregiving.

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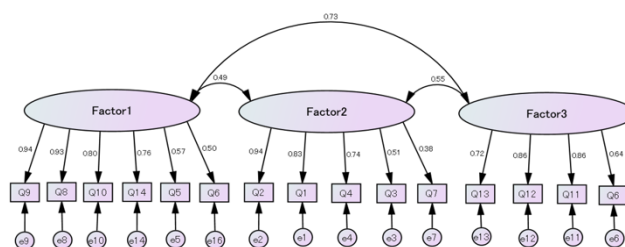
GFI＝0.807 AGFI＝0.734 CFI＝0.807 RMSEA＝0.095.

Figure 1 Confirmatory factor model of a support scale for family caregivers' appraisal

Table1   The result of Exploratory factor analysis

Factor (Cronbach's alpha) item	Factor Lodings		
	Factor1	Factor2	Factor3
Empathy and collaboration in caregiving （α=0.883)			
9 Visiting nurses understood the difficulties of daily care.	0.877	0.247	0.263
8 Visiting nurses recognized the hard work I (caregiver) put into caring for care recipient (family member).	0.84	0.204	0.323
10 Visiting nurses listened to me (caregiver).	0.682	0.307	0.294
14 Visiting nurses recognized me as being skilled in the art of caregiving.	0.669	0.099	0.364
5 I worked with a visiting nurse to care for care recipient.	0.505	0.185	0.193
16 Visiting nurses were assigned to or took over the care of care recipient in order to reduce the burden of caregiving.	0.381	0.290	0.226
Support that considers the caregiver's and family's wishes （α=0.817)			
2 Visiting nurses told me about care recipient intentions and thoughts.	0.161	0.894	0.212
1 Visiting nurses encouraged care recipient to express his/her true feelings.	0.027	0.822	0.225
4 Visiting nurses told care recipient to convey my thoughts to him/her.	0.318	0.676	0.166
3 Visitng nurses listened to care recipient about his/her likes and hobbies before he/she became ill.	0.239	0.477	0.101
7 Visiting nurse helped us to do things at home that we could not do at the hospitals or facility (e.g., hold birthday parties).	0.224	0.319	0.115
Provision of information and skills regarding the recipient's care （α=0.849)			
12 Visiting nurses explained care recipient's current condition.	0.307	0.239	0.793
11 Visiting nurses informed me about care recipient's illness.	0.344	0.279	0.709
13 Visitng nurses taught me caregiving techniques.	0.288	0.173	0.679
6 Visiting nurses established a path and direction on how to provide caregiving.	0.374	0.212	0.448
	Factor1	Factor2	Factor3
(Total α＝0.914) eigenvalue	3.46	2.80	2.42
contribution ratio (%)	23.06	18.64	16.15
cumulatjve contribution ratio (%)	23.06	41.69	57.84

Maximum likelihood and Varimax rotation

Factors Associated with Dementia Worry among Middle-Aged or Older Adults: A Literature Review

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Introduction

With an aging global population, the number of people with dementia is predicted to triple by 2050 [1]. Consequently, we should rapidly achieve not only prevention or treatment of dementia, but also a society in which people with or without dementia live together.

Accordingly, recent studies have focused on the degree of worry about developing dementia, "Dementia Worry (DW.)"

Furthermore, DW has just defined as an emotional response to the perceived threat of developing dementia and has been reported to vary from responses positioned as concern or worry to those positioned as obsessions or phobias [2]. Moreover, this study [2] found that DW was strong in British middle-aged and older adults, and 31% of British participants reported fearing dementia more than fearing other serious health problems [2]. In Germany, DW was also reported 55% had a little or some, 16% had a severe fear of dementia [3].

Some previous studies that focused on factors of people with stronger DW suggested the following: they had suicidal ideation [4], and their executive function was decreased [5]. These findings suggest the existence of people with stronger DW and obstacles in their lives, as well as the need for support. If the factors of a stronger DW can be accurately identified, effective supports can be provided to them according to the evidence.

Therefore, this literature review aimed to clarify the factors associated with DW among middle-aged or older adults.

Methods

In September 2023, we conducted a literature review using the Web of Science database, using search terms with a combination of "dementia," "worry," "anxiety," "fear," and "concern" (Figure1). We retrieved 399 articles and surveyed their titles and abstracts. Finally, we focused on articles that explored factors associated with DW and selected 12 articles for this review (Table1).
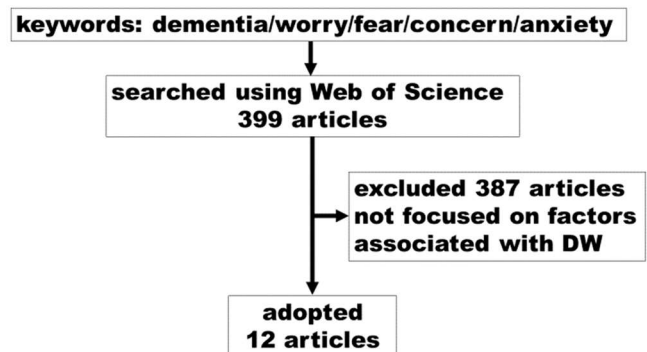

Figure1: selection of articles

Results

Our literature review revealed commonalities and differences in factors associated with DW among several countries. From this perspective, the results are as follows.

1. Commonality of factors associated with Dementia Worry

Previous studies have commonalities among several countries regarding the factors associated with DW [6, 7, 8, 9, 10, 11, 12, 13, 14].

1.1 Perception of dementia etc.

In Germany and the United States, stereotypes of dementia or aging, such as the belief that dementia ruins their lives, are associated with DW [6, 7]. Similarly, prejudices and ageism are associated with it among the Chinese and Israelites [8, 9].

1.2 Psychological health status

Depression, loss of motivation, psychological distress and insomnia are associated with DW among the Americans, Koreans, Germans, and Chinese [10, 11, 12, 13]. In addition, concerns about one's own memories and perceived memory changes are associated with DW in the United States, Korea and Germany [10, 11, 12].

1.3 Social background

Exposure to people with dementia and a family history of dementia is associated with DW in Americans and Koreans [10, 11]. In addition, decline in family functioning or attachment and unmarried among Chinese and Korean is also associated with DW [8, 14].

Table1: Articles about factors associated with DW.

Country	Year	Reference No.
the United States	2016	[10]
	2017	[7]
	2020	[4]
	2021	[5]
Germany	2019	[12]
	2020	[3]
	2020	[6]
Korea	2019	[14]
	2021	[11]
China	2022	[8]
	2023	[13]
Israel, Australia	2022	[9]

2. Differences of factors associated with Dementia Worry

On the other hand of the above commonality, previous studies conducted in various countries have revealed differences in the factors associated with DW [3, 8, 10, 11, 12, 14].

2.1 Age

For the all-age groups over 40 years old, DW was generally strongest in the 50–70 age group and weaker in the younger age group of 40 years old and the older age group of 80 years and older; it resembled mountain-shaped curve for Germans [12]. Furthermore, for all ages 18 and older, DW was the strongest among 45–64-year-olds in China [8]. Although several studies have generally found an association between middle to early age and DW, as in these two articles, age was not associated with DW for Americans [10].

2.2 Sex

In contrast to the stronger DW in females among Germans [3], sex was not associated with DW among Americans [10].

2.3 Health status

Although having chronic diseases were associated with stronger DW among Koreans [11], physical health was not associated with DW among Germans [12].

2.4 Educational background

In Korea, one study reported that higher school education was associated with stronger DW [11], while another reported that lower school education was associated with stronger DW [14].

Discussion

Although some aspects of the factors associated with DW have been clarified, several factors show conflicting results in different backgrounds. This suggests that DW is related to physical, psychological, and social factors in a complex manner. Moreover, despite the accumulation of previous studies in a wide range of countries, including Europe, the United States, and Asia, we have not yet established a theory that can explain the factors associated with DW. Further research is needed to support people with strong DW based on scientific evidence.

In particular, Japan has already witnessed rampant aging and the aging rate is approximately 30%, the highest in the world [15]. The number of people with dementia is expected to further increase. When the factors associated with DW among Japanese people are clarified, these results can become scientific evidence for effective care for people whose lives are affected by DW, and we will be able to recommend this to society.

Japan needs to lead the world in developing measures against DW or supporting people suffering from it and share the results with other countries to contribute to the world.

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Factors related to nurse turnover Intention: A literature review

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Introduction

Nurse turnover intention has a significant impact on the quality of patient care, the financial costs borne by hospitals, productivity, and the job satisfaction of nursing staff. This issue is a major concern for healthcare organizations (1). High turnover rates among nurses have been associated with negative impacts on patient safety and care continuity (2), as well as significant financial burdens related to recruitment, orientation, and training of new staff (3). In addition, frequent turnover can reduce morale and job satisfaction among the remaining nursing workforce, potentially leading to burnout and decreased overall staff retention (4). Nurse turnover in hospitals is also recognized as a problem in Mongolia. The aim of this review is to evaluate the current literature to identify factors related to nurse turnover intention.

Methods

Studies from CINAHL, ProQuest, PubMed, and Embase were included. The review was conducted between January 2013 and January 2023 to ensure the inclusion of up-to-date information on the issue. The search terms used combinations of keywords such as "nurse turnover" and "turnover intention."

Results

Initially, 827 studies were retrieved and abstracts were screened for content relevance, resulting in the inclusion of 14 studies in this summary review (Figure 1). All 14 studies (5-8) in this review used a cross-sectional research design with observational methodologies. These studies encompassed various countries, including China, Iran, South Korea, Japan, the United States, and others. The sample sizes of nurses in these studies ranged from relatively small samples of around 133 participants to larger cohorts exceeding 17,582 nurses. Factors related to nurse turnover were divided into two categories: individual and organizational factors. The individual factors were further identified as biopsychosocial and job-related factors.

Figure 1. Flow chart of study selection
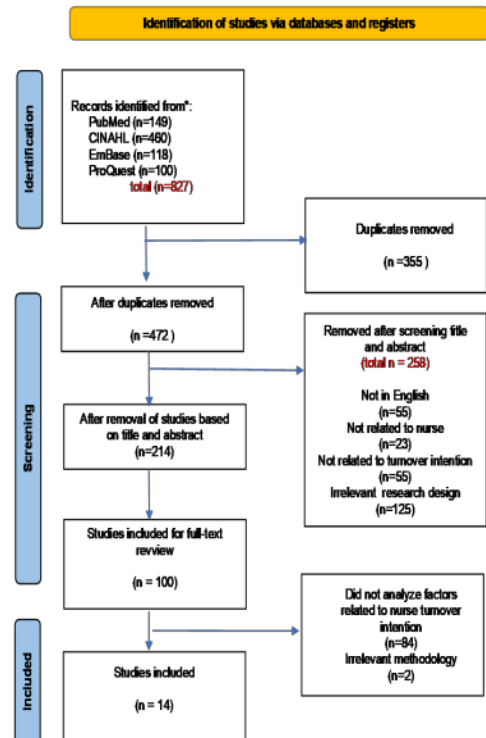
Discussion

Among individual factors, biopsychosocial elements such as age, gender, education level, and sleep disturbances have been found to influence nurse turnover. Additionally, job-related factors like job stress, satisfaction, and burnout are also linked to turnover. To reduce nurse turnover, hospitals need to take into account these biopsychosocial factors and implement interventions aimed at reducing occupational stress and burnout. Organizational factors that have been identified as influencing nurse turnover include cultural aspects such as organizational leadership, professional opportunities, and conflicts. As such, it is crucial to shift the hospital's organizational culture in a positive direction. Healthcare organizations in Mongolia must acknowledge the importance of identifying and addressing these related factors in order to maintain a stable and satisfied nursing workforce.

Conclusion

Nurse turnover intention is a multifaceted issue that warrants further investigation and understanding. It is crucial to identify and address the diverse factors contributing to nurse turnover intentions, as this knowledge can inform the development of effective strategies. These strategies can significantly influence healthcare organizations and the quality of patient care. Consequently, ongoing research and interventions that consider a range of factors are necessary to mitigate the issue of nurse turnover in Mongolia.

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Factors related to nurses' organizational commitment: A literature review

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Introduction:

Organizational commitment (OC) is a crucial element in the nursing field, significantly impacting nurse turnover and work-related outcomes [1]. This concept is multifaceted, with both attitudinal and behavioral perspectives playing a role [2]. The attitudinal perspective emphasizes an employee's identification with the organization and their aspiration to sustain a long-term relationship [3]. Conversely, the behavioral perspective characterizes OC as an individual's commitment to the organization, demonstrated by the personal time they devote to organizational activities [4].

Mowday et al. [5] defined OC as "the relative strength of an individual's identification with and involvement in a particular organization." Optimal nursing performance depends upon the knowledge, competencies, job satisfaction, and OC of individual nurses [6].

Recognizing that factors related to OC may evolve over time due to changing roles in nursing [7], it is crucial for nurse managers to understand the factors influencing OC within the current nursing workforce. This review aims to evaluate these determinants as presented in the current literature, shedding light on the multifaceted nature of nurses' OC in hospital settings.

Purpose

This study was conducted to identify and describe the factors relating to nurses' OC in published nursing research.

Method

Study Design: This study conducted a thorough review of the research literature to comprehensively investigate the factors related to nurses' OC.

Data Sources: The research commenced with an extensive search strategy across four major electronic databases: CINAHL, Embase, PubMed, and Cochrane. This choice of databases was designed to guarantee a thorough and exhaustive investigation of the pertinent academic literature, using the key terms "organizational commitment" and "nurses."

Inclusion Criteria: To ensure the inclusion of up-to-date and relevant research, this literature review considered studies that met the following criteria:

1. Publication from 2013 to 2023, thereby encompassing recent developments in the field.

2. Focus on investigating factors that influence or are related to nurses' OC.

3. Studies published in the English language.

4. Studies that used a cross-sectional design

Data Collection: A systematic and rigorous data collection process was conducted for all studies meeting the aforementioned inclusion criteria. This involved the comprehensive extraction of pertinent information from these studies.

Final Sample: The systematic search across four electronic databases yielded a total of 663 studies relevant to the study topic. Following the application of the inclusion criteria, as well as the completion of data extraction and analysis, the ultimate sample for this review consisted of a total of 13 studies. These studies met the inclusion criteria and provided valuable insights into the factors relating to nurses' OC within the specified timeframe (2013-2023).

Data Analysis: The data extracted from the selected studies were meticulously and thoroughly analyzed. This process entailed the systematic categorization of findings pertaining to factors related to nurses' OC.

Figure 1: Flow chart of article selection for the review.
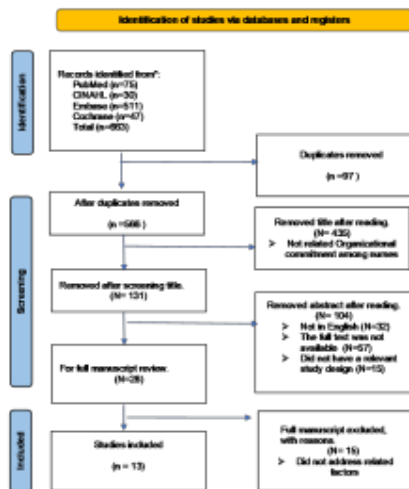
Results:

1. Characteristics of selected articles

The selected papers were categorized based on several characteristics, including the author, year of publication, country of origin, sample setting, variables, and significant factors.

2. Relevant characteristics according to category

2.1 The significant personal characteristics were age, gender (male), years of experience (5), religion (Muslim), participation in an ethics course, departmental affiliation, monthly income, average hours of sleep per day, level of dedication, job satisfaction, passion, psychological empowerment, self-determination, alignment with the organization's values (person-organization fit), perceived overqualification (viewed negatively), symptoms of anxiety (also viewed negatively), and psychological capital.

2.2 The organizational characteristics were promotion (-), perceived empowerment, organizational climate, supervisor social support, vigor, absorption, internal marketing, learning organization, and structural empowerment.

Conclusion:

In this review, we analyzed 13 out of identified 663 studies to gain insight into the factors influencing nurses' organizational commitment from 2013 to 2023. Notable factors include job-related elements such as job satisfaction, and psychosocial factors like psychological empowerment, psychological capital, and structural empowerment. Healthcare organizations should concentrate on these areas to boost nurses' commitment, taking into account cultural and psychosocial variations. This review provides valuable guidance for enhancing nurse commitment, which benefits both healthcare systems and patient care. The studies selected for this review collectively contribute to a more profound understanding of the intricate dynamics surrounding nurses' commitment to their organizations. Further research should continue to track these commitment dynamics beyond 2023. There is also a need for future research on the psychosocial variables that influence nurses' organizational commitment.

The limitation to studies published solely in English suggests that we may have missed some valid research. Further investigation is required into the psychosocial factors influencing nurses' commitment to their organizations.

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Generations of Nurses in Korea: A Scoping Review

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1. Introduction

According to a 2021 report published by King's College in the UK, Korea ranked first among 28 OECD countries in ideological, rich, gender, academic, political, generational, and religious conflicts, and Korea's generational conflict is high among OECD countries. According to a recent 2023 survey conducted by Korea Research, 80% of people felt that the generational conflict was serious, and 49% felt that the seriousness of the generational conflict would be similar or increasingly serious, up from 43% in 2022[1]. In addition, according to a 2020 survey conducted by the Korea Chamber of Commerce and Industry, 6 out of 10 workers (63.9%) of 30 large and medium-sized companies feel the generation gap, and the degree to which the generation gap negatively affects their work has increased[2]. Over the past decade, as interest in generational conflicts has increased in various fields, studies on generational differences and generational conflict among nurses in hospitals have also increased. However, literature review studies on generations of nurses in Korea were insufficient. Therefore, it is necessary to examine research related to on generations of nurses in Korea and to identify overall research to find ways to resolve generational conflicts in the organization.

2. Purpose

This study aims to understand the general characteristics, research methods, related variables, and characteristics of research results of the study on generations of nurses in Korea through a scoping review.

3. Methods

The research process was conducted to the five steps of Arksey and O'Malley(2005). The data were searched based on PubMed, Cochrane, CINAHL, EMBASE, KMBASE, KoreaMed, KISS, KISTI, NDSL, RISS, and DBpia. Studies published up to August 2023 were included. The selected 8 studies were organized using Zotero and Microsoft Excel.

4. Results

1) General Characteristics

The final selection of 8 studies revealed that there were no publications between 2013 and 2019. However, there were 4 studies published from 2020 to 2022 and another 4 studies published in 2023.

2) Research Design and Purpose

A total of 8 studies were all quantitative research, consisting of 3 descriptive survey studies, 4 descriptive correlational studies, and 1 structural model validation study. The purposes of each study were as follows: 3 studies aimed to elucidate generational differences, 3 studies investigated the correlations among variables related to generations, 1 study aimed to identify factors influencing generational conflict in organization, and 1 study focused on constructing a structural model and validating the structural relationships among variables.

3) Participants Characteristics

The sample sizes ranged from 97 to 560. The participants were classified into generations based on their birth years in a total of 7 studies. Among them, 6 studies made distinctions between X, Y, and Z generations as criteria, while 1 study used the MZ generation as a criterion. There was 1 study that did not specify the criteria for generational classification.

4) Variables, Analysis Methods, and Research Results

The study encompassed a total of 20 variables related to Korean hospital nurses' generations. Among these variables, the most frequently mentioned were Work Values and Organizational commitment, each covered in three studies.

Regarding the research methods, all eight selected articles employed non-experimental research designs, consisting of five multiple regression analyses, one correlation analysis, one chi-squared test, and one structural equation modeling analysis.

When looking at the study results, a total of seven studies examined generational differences by distinguishing between generations based on birth years. Among these, X-generation nurses showed higher Job Satisfaction and Organizational Commitment than Y and Z-generation nurses. Additionally, X-generation nurses exhibited a preference for intrinsic Work values and considered family life and work to be important. Furthermore, X-generation showed higher Professional pride and Organizational Commitment than Y- and Z-generation. In contrast, Y and Z-generation nurses exhibited a significant positive correlation between Work Values and Job Satisfaction, primarily favored extrinsic Work values, and tended to prioritize leisure time. They also placed more importance on interest in their work compared to X-

generation nurses. Additionally, higher education levels, specifically postgraduate education, were associated with increased Job Embeddedness. The factors affecting Retention Intension were found to be Job Embeddedness, Nursing Practice Environment, and Job Esteem.

Among X and Y-generation nurses, their communication Types were found to be more similar to each other than to those of Z-generation nurses. X and Y-generation nurses also tended to prioritize family life. In the case of Z-generation nurses, Emotional Labor and Burnout were found to have a greater impact on their Organizational Commitment compared to X and Y-generation nurses.

Across all generations, Job Satisfaction and Organizational Commitment displayed a strong positive correlation. Factors such as financial benefits, job security, and working environment were considered important. Furthermore, Social Support was identified as the most significant influencing factor on Organizational Commitment.

5. Discussion

The limitations of this study include the very limited number of final selected documents and the fact that the PRISMA protocol guidelines were not followed in the literature selection process. Furthermore, in the case of the scoping review, the absence of the ability to evaluate the quality of the literature may affect the validity and reliability of the research results. However, this study has significance in exploring the scope and diversity of the research through the scoping review, providing a broader understanding of research topics and issues. Additionally, it thoroughly examined the trends in research on the generational differences among hospital nurses in South Korea, including the methods used for generational categorization and the relevant variables. Moreover, the study's value lies in providing evidence and directions to mitigate intergenerational conflicts in organizations.

6. Conclusion

This study suggests various approaches such as qualitative research, literature reviews, and intervention studies in research related to generations of Korean hospital nurses. Secondly, there is a need for research approaches that can distinguish generations through clear terminology definitions and conceptual modeling. Thirdly, it is necessary to investigate how the variables that reflect generational differences among Korean hospital nurses actually impact generational conflict in organization. Furthermore, this research emphasizes the importance of nursing organizations in understanding generational differences, resolving intergenerational disconnects and conflicts, and fostering a supportive nursing practice environment and organizational culture to enhance job satisfaction and organizational commitment.

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Radiological Science/Radiological Technology: Lecture room-1 （Main building 2F）				
13:30 〜 14:30	Chair	Prof. Hirano Yoshiyuki	Nagoya	Presentation: 10 min, discussion and questions: 5 min
		Jehyeong Yeon	Yonsei	Removal of gradient and pulse artifacts in simultaneous EEG-DTI data acquisition: An AAS and ICA approach
		Habin Kim	Yonsei	Radiation-Hardened Preamplifier Design for Radiation Detector
		Ji Won Choi	Yonsei	Investigation of fetal dose from carbon radiotherapy during pregnancy - Monte Carlo study
		Yoon Soo Chung	Yonsei	Directional radiation monitoring system using Artificial Neural Network
14:30 〜 14:40	10-minute break			
14:40 〜 15:40	Chair	Prof. Chul Hee Min	Yonsei	Presentation: 10 min, discussion and questions: 5 min
		Aoyama Kanako	Nagoya	Evaluating nanoparticle candidates as radiation modifiers on DNA damages for radiation therapy
		Jiyong Shim	Yonsei	New Method for Dental Panoramic Reconstruction Using Cone-Beam Computed Tomography Projection Data
		Honjou Haruto	Nagoya	Simulation study of a bent crystal based monochromatic X-ray imaging with an X-ray tube
		Soo Min Lee	Yonsei	Study on the Sewage Sludge Reduction and Solubilization Depending on Dose of Gamma Irradiation

Removal of gradient and pulse artifacts in simultaneous EEG-DTI data acquisition: An AAS and ICA approach

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Introduction

The glymphatic system(GS) is a waste clearance system in the human brain that utilizes the influx of cerebrospinal fluid (CSF) into parenchyma during sleep [1]. The intratissue influx of CSF affects the diffusion properties of the brain tissue. Therefore, diffusion tensor imaging (DTI) is a usful technique for non-invasively monitering the function of GS

Dynamic monitoring of GS function using DTI requires information about the patient's sleep stages at the time of the DTI data acquisition. This requires simultaneous acquisition of DTI and electroencephalgraphy (EEG).

However, simultaneous EEG-DTI is accompanied by significant challenges, particularly in the quality of EEG signal. Prominent among these challenges are the gradient artifact (GA) and pulse artifact (PA). The GA is induced by the rapid switching of gradient magnetic fields in MRI, with intensity being 10 to 100 times larger than that of the EEG signal [2-4]. Concurrently, the PA is caused by electrode movements within the strong static magnetic field, influenced by the subject's pulsating scalp and blood flow [5-7]. The average artefact subtraction (AAS) technique has been widely used for the removal of GA in simultaneous EEG-fMRI.

In this study, in order to use for identifying sleep stages, we studied GA and PA removal from EEG signals measured in simultaneous EEG-DTI using AAS and Independent Component Analysis (ICA).

Methods

Participants (male, n = 4, age = 20 – 30) were subjected to sleep deprivation. To facilitate the onset of sleep within the MR environment, participants were administered a sedative.

EEG signals were measured outdie the MRI scan room for 90 s for artifact-free EEG signal (EEGo). During the experiment, EEG signals were measured continuously and fifteen DTI scans were performed, each scan after 90-second rest. EEG signal simultaneously measured with DTI (EEGd) and EEG signal measured during 90-second rest (EEGr) were acquired.

GA and PA removal algorithms that incorporate the approach proposed in [5] were included in in-house-developed MATLAB software (R2023a, MathWorks, Natick, MA, USA). Given the inherent synchronization challenges between EEGd, an novel synchronization approach was used. The first EEGD was designated as the reference. An arbitrary point within this EEGD was picked, and subsequent EEGd was then correlated with this reference. The starting point of each epoch was identified by pinpointing the maximum correlation to the reference, ensuring optimal alignment. Post synchronization, AAS technique was employed to remove GA from EEGs. To remove the PA from EEGs and EEGr, we employed ICA to accurately isolate and eliminate them.

After artifact removal, the resulting EEGd were evaluated using spectral anlaysis. Since we analyzed EEG signals measured in sleeping state, the EEG signal power ratio of EEGd and EEGo were calculated for delta (1 – 4 Hz), theta (4 - 7.5 Hz), alpha (8 – 14 Hz), and beta (14 – 30 Hz) waves.

Results

Table 1 shows the power spectral distribution ratios of the Delta, theta, Alpha and Beta for each subject. Theta and Alpha waves show a ratio close to 1, indicating that GA and PA were well removed. To minimize the difference between subjects, all epochs without GA and with removed GA were compared. The results for a total of subjects were delta wave: 0.443, theta wave: 0.818, alpha wave: 0.968, and beta wave: 1.448.

Table. 1: Power spectral distribution ratios of the EEG signal after AAS and ICA processing and the artifact-free EEG signal GA for each subject.

	Delta	Theta	Alpha	Beta
Subject 1	0.992	0.652	0.277	1.000
Subject 2	0.113	1.000	1.717	0.735
Subject 3	0.236	0.997	0.751	3.058
Subject 4	0.429	0.621	1.129	0.999
Total	0.443	0.818	0.968	1.448

Discussions

Simultaneous EEG/DTI measurements are essential to monitering the GS function. In this study, we employed both the AAS and ICA techniques to remove the artifacts in EEG signal generated during simultaneous EEG/DTI measurements.

We focused on delta, theta, alpha, and beta waves, which are essential for determining sleep states.

The power distribution of theta and alpha waves indicates that GA and PA were well removed in the delta and theta waves. the possibility of accurately

identifying sleep stages through EEGs. However, there may be differences in low-frequency delta waves from person to person. If the onset timing of the gradient field is different for each EEGd, GA removal may not be effective above 15 Hz. When EEG-DTI is measured simultaneously, the onset time of the gradient pulse is not recorded, synchronizing the onsets of the GA signals. However, the proposed method pinpoints the starting signal of the gradient pulse and effectively remove both GA and PA, especially below 13 Hz. If large residual artifacts remained despite GA removal, they were sometimes mistaken for beta waves. It has been reported that residual artifacts in GA can be effectively removed by increasing the number of EEGd [5]. Therefore, this study suggests that sleep stages can be identified from the artifact-removed EEGs using the proposed method if the number of simultaneous EEG-DTI increases to greater than 25.

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Radiation-Hardened Preamplifier Design for Radiation Detector

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1. Introduction

In an era where electronic devices have become indispensable components of our daily lives, the demand for reliable, high-performance circuits has reached unprecedented levels. Whether it's for communication, data processing, medical instrumentation, or space exploration, electronic systems must not only function flawlessly but also endure the harshest of environments. One such challenging environment is radiation, which encompasses a spectrum of ionizing and non-ionizing radiation sources, including cosmic rays, solar radiation, and terrestrial radiation.

The effects of radiation on electronic circuits can be detrimental, leading to data corruption, device malfunctions, and even complete system failures. In critical applications, such as those in aerospace, nuclear facilities, and medical devices, the need for radiation-hardened circuits is paramount. This has sparked a thriving area of research and development dedicated to the design and optimization of radiation-resistant electronic circuits. This paper delves into the realm of radiation circuit design, addressing the unique challenges and opportunities it presents. We explore the fundamental principles, strategies, and innovations that enable circuits to operate reliably in radiation-rich environments. With a focus on both ionizing and non-ionizing radiation, we aim to provide a comprehensive overview of the current state-of-the-art in radiation-hardened electronics. We researched a study on radiation-hardened by design (RHBD) preamp design using binary weighted current source (BWCS).

2. Methods

The radiation hardening strategy involves using a 6-bit BWCS to compensate for changes in the current level of the preamplifier to minimize the total ionization dose (TID) effect. This preamp is designed using a two-stage operation amplifier (OP-AMP), which features low power, low noise, high speed, and proper gain.

The preamp proposed in Fig. 1(a) is designed to compensate for the TID effect. In addition, the configuration of the OP-AMP consisting of the same circuits as the CSA is used for the proposed pre-amp consisting of self-bias circuits, transmissions. The gate
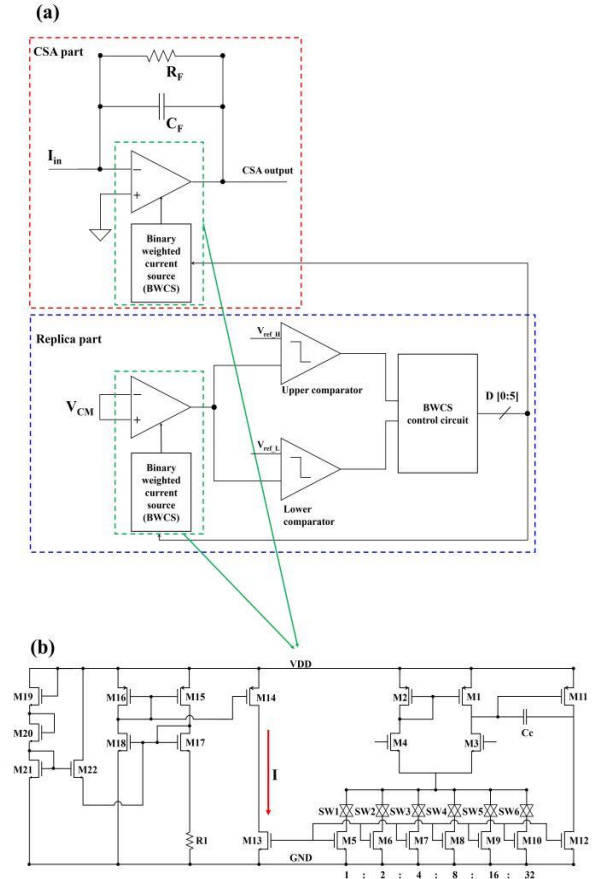

Fig. 1 (a) Block diagram of proposed preamplifier. The proposed preamplifier consists of two parts: the CSA and replica. (b) Configuration of two-stage OPAMP used for proposed preamplifier. The OPAMP has a 6-bit binary weighted current source (BWCS) to compensate for TID effects.
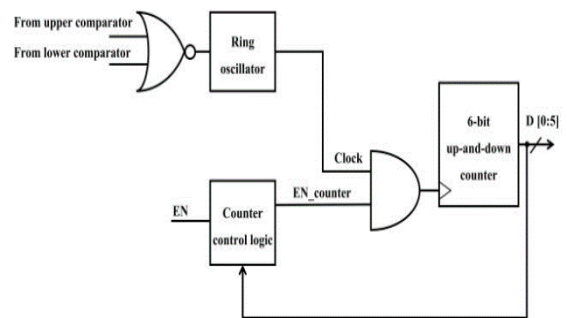

Fig. 2 Configuration of the BWCS control circuit. The circuit consists of a ring oscillator, counter control logic, and a 6-bit up-and-down counter.
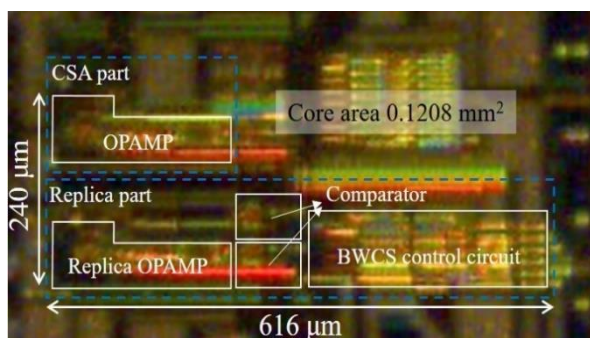
Fig. 3 Photograph of the proposed preamplifier circuit in 0.18μm standard CMOS technology.

Table 1
Electrical parameters of the two-stage OPAMP with 6-bit BWCS.

Parameters (unit)	Value
Supply voltage (V)	1.8
Miller capacitance (pF)	1
Open loop gain (dB)	66
3dB BW (kHz)	112.5
GBWP (MHz)	217.15
Phase margin (°)	55

contains a 6-bit BWCS, as shown in Figure 1(b). RHBD techniques can significantly improve the performance of the system in a radiation environment. The BWCS circuit consists of a ring oscillator, a 6-bit up-and-down counter, and control logic, as shown in Fig. 2. Depending on the output signal from the BWCS circuit, supply current to the OP-AMP at the proposed pre-amp in the range of 1I to 64I. By self-compensating techniques for this current, the pre-emp can mitigate changes in current induced by radiation effects.

The RHBD preamplifier was implemented in a general-purpose complementary metal-oxide-silicon field effect transistor (MOSFET) 0.18μm technology process. A photograph of the fabricated chip is shown in Fig. 3. The active area of the proposed circuit occupies 0.1208 mm^2. Table 1 lists the electrical specifications of the OP-AMP for the proposed preamplifier.

3. Results and Discussions

The verification test was conducted by the Korea Atomic Energy Research Institute (KAERI) using cobalt-60 gamma-rays at a rate of 10.46kGy (SiO$_2$) at a rate of 230kGy (SiO$_2$)/h. Experiments showed that the digital code had a maximum value of 42 and a minimum value of 29 while the initial value was 39 before the test. The results indicate that the system current level tends to decrease as a result of radiation effects. This phenomenon might have been related to the leakage current increase. When the leakage current
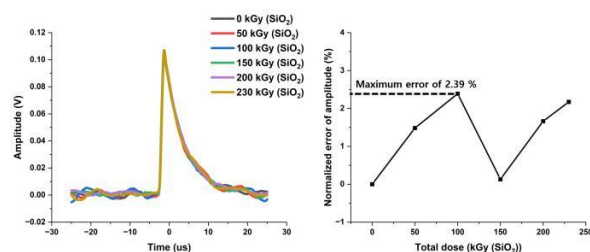
Fig. 4 During irradiation test with gamma rays up to 230kGy (SiO2):
(a) recorded output of CSA and
(b) error rate of normalized amplitude of the preamplifier obtained as a maximum error rate of 2.39%

increased, the system current level also increased. Thus, the BWCS was able to decrease the system current.

Fig. 4 shows the output of the preamp at 50kGy (SiO$_2$) intervals during the test. Changes in the output amplitude may result from changes in the open-loop gain. The open-loop gain was determined by the transconductance and output resistance of the OP-AMP. Fig. (b) depicts the error rate of the normalized maximum amplitude of the proposed preamplifier. A maximum error of 2.39% was observed at 100kGy (SiO$_2$), with the digital code reaching 38.

4. Conclusion

The RHBD preamplifier can mitigate radiation induced degradations, particularly TID effects, by compensating the tail current of the OPAMP used for the preamplifier using a 6-bit BWCS, through which a wide range of current (1I to 64I) can flow. The replica OP-AMP of the proposed preamplifier detects the changes in the operating point caused by the total radiation dose and generates a signal to control the BWCS, aiming to minimize TID effects. The circuit was fabricated using the 0.18μm CMOS process, and occupied 0.1208 mm^2. An irradiation test was performed using a gamma-ray source up to 230kGy (SiO$_2$) at a rate of 10.46kGy (SiO$_2$)/h. The RHBD preamplifier could be used in various sensor applications, particularly radiation environments, because the proposed circuit could maintain its performance regardless of increased radiation exposure.

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Investigation of fetal dose from carbon radiotherapy during pregnancy
- Monte Carlo study

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Introduction

Radiotherapy for pregnant cancer patients is considered when it is essential for the primary treatment, or when surgery and/or chemotherapy are insufficient [1]. Compared to conventional photon therapy, particle therapy using proton or carbon ion beams, which can improve dose conformity to the target by their unique dose distribution (i.e., Bragg peak), may provide a better focus on the tumor region of the mother and reduce the dose for fetus [2]. A successful case has been reported in which proton therapy for craniospinal irradiation (CSI) was administered to a pregnant woman with an atypical teratoid/rhabdoid tumor [3]. Recently, a Monte Carlo (MC) study was conducted to systematically quantify the amount of the fetal dose contributed by secondary particles (neutrons and photons) produced by the interaction of the proton beams within the body of the mother treated with the CSI [4].

Radiotherapy with carbon ion beams which have a sharper Bragg peak than proton beams has been recently getting more attention. Carbon ion therapy, therefore, can be also considered applicable for the CSI treatment to pregnant patients while the detailed information of the fetal doses is yet to be reported. To fill this gap, we investigated fetal organ doses from carbon beam CSI during pregnancy by performing MC dose calculations and compared to the fetal doses estimated for the proton CSI in the previous study [4].

Methods

We employed the high-quality pregnant female phantom series developed by University of Florida (UF) for eight gestational ages (8, 10, 15, 20, 25, 30, 35, and 38 weeks) [5, 6]. The phantoms were converted into DICOM-RT (Digital Imaging and Communications in Medicine – Radiotherapy) format by using a conversion program, DICOM-RT generator [7]. The converted DICOM-RT data were implemented into a treatment planning system (TPS) with a prescribed dose of 36 Gy to create a carbon CSI plan, as shown in Fig. 1. TPS dose distributions on the pregnant phantoms for 25-week from carbon therapy are shown in Fig. 2. The carbon CSI plan (CT and beam information) for each gestational age was simulated by performing TOPAS (Tool for Particle Simulation) MC based dose calculation system that were commissioned to the carbon beam measurement data. We computed organ/tissue-averaged absorbed doses for the following 28 organs of the fetus: bone, lungs, colon, stomach, breasts, testes, ovaries, urinary bladder, esophagus, liver, thyroid, brain, salivary glands, skin, adrenals, extrathoracic (ET) region, gall bladder, heart, kidneys, muscle, oral mucosa, pancreas, small intestine, spleen, prostate, uterus, thymus, and eye lenses.
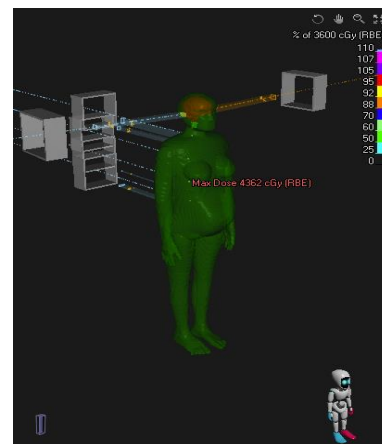

Fig 1. 3D view of 25-week pregnant phantom implemented in treatment planning system where carbon CSI is being planned.

Results & Discussion

The fetal whole-body dose for each gestational age ranged from 6 mGy (30-week) to 99 mGy (20-week). The organ/tissue doses for the 20 weeks showed the largest variation ranging 7 mGy (thyroids) to 99 mGy (prostates), while the doses for 8 weeks showed the smallest variation ranging from 21 mGy (gall bladder)

to 30 mGy (brain). Table 1 shows the average, minimum, and maximum doses for each gestational age.
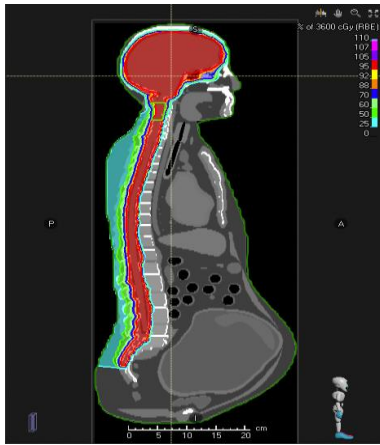

Fig 2. Dose distribution on 25-week pregnant phantom as a result of CSI plan using the TPS.

Table. 1: Fetal average doses, minimum doses, and maximum doses for Carbon Ion Therapy.

Gestational age	Average dose [mGy]	Minimum dose [mGy]	Maximum dose [mGy]
8-week	26	21 (gall bladder)	30 (brain)
10-week	17	11 (lung)	28 (brain)
15-week	24	7 (oesophagus)	47 (bladder)
20-week	37	7 (thyroid)	99 (prostate)
25-week	20	6 (oesophagus)	31 (small intestine)
30-week	28	6 (oesophagus)	58 (small intestine)
35-week	37	13 (oesophagus)	88 (lens)

Figure 3 shows the comparison of fetal organ doses between carbon ion therapy and proton therapy for each gestational age. All the fetal organ doses from carbon therapy were greater about 1.5 times to 47.3 times than those from proton therapy
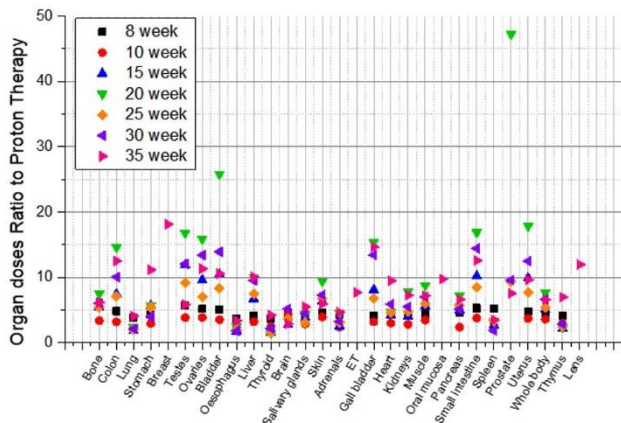
Figure 3. Fetal organ dose ratios between carbon ion therapy and proton therapy for each gestational age

Nevertheless, when accounting for the total process in carbon therapy, including CT and X-ray scans, the average fetal dose was 91.5 mGy while the threshold of 100 mGy for significant risk of damage for the fetus is recommended by AAPM Report No. 36 [8].

Conclusion

We conducted MC simulations of the carbon PBS CSI on pregnant computational phantoms that include high-quality fetal models and a TOPAS MC beam commissioned to the carbon measurement data. Considering the rapid expansion in carbon therapy centers around the world, the result of the present work would be considered as the informative data for one to estimate dose to the fetus as one of the first clinically informative predictions just in cases that carbon therapy during pregnancy should be considered urgently.

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Directional radiation monitoring system using Artificial Neural Network

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Introduction

In January 2023, a radiation capsule containing ^{137}Cs was lost during transit in Australia. ^{137}Cs has a half-life of about 30 years, which could cause overexposure damage to public if it went undetected or lost permanently. In the event of such a radiation accident, it is crucial to minimize the damage by detecting radioactive material early, thereby protecting public health and preserving the environment. Therefore, the location of radioactive material must be rapidly detected in order to take necessary actions [1].

A radiation detector capable of determining the direction of the radioactive source is necessary to quickly and efficiently detect the location of radioactive material. However, conventional directional radiation monitoring systems have the disadvantages of long measurement time due to a narrow field of view and reduced accuracy of direction information for long-distance radioactive sources [1-3].

Thus, a new structure of directional radiation monitoring detector is proposed to compensate for the limitations of conventional detectors. The proposed detector is composed of four detector modules with externally attached wall-type collimators. The field of view of each detector module varies with the source direction due to the geometry of wall-type collimator. The count obtained from each detector module varies according to the location of the source. To detect directional information of the source, the count difference between detector modules was analysed using an artificial neural network algorithm (ANN).

In this study, we evaluated the performance of the proposed directional radiation monitoring system. The proposed detector was designed and optimized using Monte Carlo simulation. The acquired data was used as training, testing and validating datasets. The performance of proposed detector and ANN algorithm was verified by analysing the accuracy of source direction detection.

Methods

As shown in Figure 1, the directional radiation monitoring detector consists of four NaI(Tl) detector modules (Φ 3" $\times$ 3") arranged in a counterclockwise direction with a wide field of view of 360 degrees. The wall-type collimator attached to the outside of the system was designed with 2 cm thick lead to cover a photomultiplier tube (PMT). Due to this structure, each detector module acquires a different gamma count according to the direction of radiation incidence. Additionally, the use of the wall-type collimator improves the accuracy of direction information of radioactive source located at a long-distance.
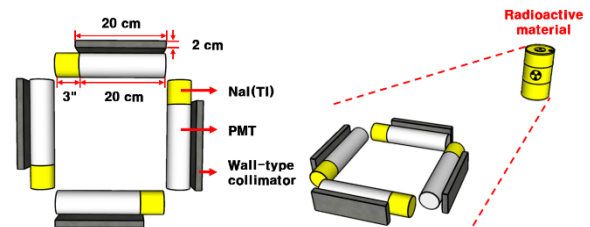

Fig. 1. The geometrical structure of directional radiation monitoring detector

The training and validation datasets of the ANN was generated using the Geant4 Application for Tomographic Emission (GATE) simulation toolkit [4]. The simulations were performed by moving the ^{137}Cs (662 keV) source from 0 to 90 degrees at 5-degree intervals around the system, as shown in Figure 2. The distance between the source and system was set to 50 m, 100 m, 200 m, and 400 m, respectively. The gamma count was acquired with a 20% energy window at the source energy peak.
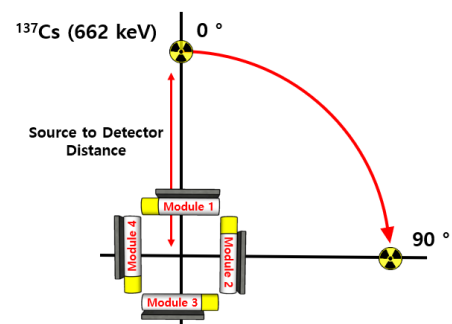

Fig. 2. Simulation conditions for obtaining count of each detector module according to the source direction

The ANN based algorithm was developed using the Python programming language. A total of 1,200 datasets were used for training and validation. The datasets were divided with a ratio of 70% for training and 30% for validation, respectively. The ANN algorithm consists of four input-layer nodes, 256 hidden-layer nodes, and one output-layer node. The activation function of the hidden layer was set to a ReLU function. The training and validation were conducted based on the settings described above.

Results

Figure 3 shows the count rate of each module according to the position angle between the source and the detector modules at a distance of 50 m. The obtained patterns were confirmed to have the same trend for other distances.
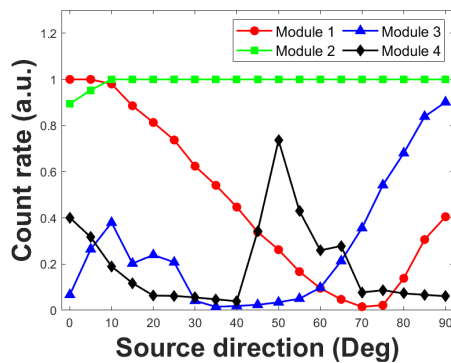
Fig. 3. The count rate of each module in the source direction

The Mean Absolute Error (MAE), a measure of a trained neural network's performance, was calculated to be 0.57. Figure 4 shows the result of predicted angle of the source direction. The predicted angles, based on the validation datasets obtained at 5-degree intervals, showed a maximum error angle of 3.54 degrees.
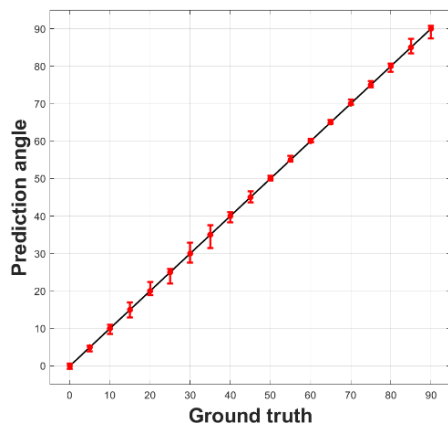

Fig. 4. Correlation between predicted value and ground truth

Discussions

In this study, we designed and evaluated the performance of the directional radiation monitoring system composed of four NaI(Tl) detector modules arranged in a rectangular shape with externally attached wall-type collimators. The proposed system was utilized with the ANN based algorithm to quickly locate the direction of a radioactive source.

As a result of the study, it was verified that the proposed detector has a different count rate for each module depending on the direction of the radiation source. The ANN was shown to have an average error of 0.57 degrees for all datasets obtained at 5-degree intervals, and was evaluated to be able to detect the direction of the radioactive material with an error of at least 5 degrees. The results show that the proposed directional radiation monitoring system is feasible.

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Evaluating nanoparticle candidates as radiation modifiers on DNA damages for radiation therapy

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Introduction

Gold nanoparticles (AuNPs) have emerged as promising radiosensitizers for medium- and high-energy photon therapies, such as γ-ray radiation in high-dose-rate (HDR) brachytherapy. However, achieving a clinically significant dose enhancement necessitates using high AuNP concentrations. Our prior research showed that the impact of positively (+) charged AuNP on radiosensitization of plasmid DNA damage induced by 192Ir γ-rays [1] and MV X-rays [2] at low concentrations, with a focus on DNA targeting (Fig.1). The dose enhancement achieved with low concentrations of +AuNPs is believed to be a consequence of DNA binding or increasing local +AuNP concentration proximate to the DNA. This study evaluated the radiosensitization effects of +AuNPs on plasmid DNA damage induced by therapeutic particle beams, such as carbon ions and protons. The selection of plasmid DNA assays for in vitro investigations was predicated on their heightened sensitivity and capacity to facilitate the straightforward detection of DNA damage [3].

Methods

We observed DNA breaks when using low concentrations of AuNPs. The pBR322 plasmid DNA, exposed to 64 ng/ml AuNPs, was subsequently irradiated with carbon ion beams (290 MeV/u) at a 6 cm spread-out Bragg peak facility located at the National Institutes for Quantum and Radiological Science and Technology (QST). We employed 5- and 30-nm +AuNPs and -AuNPs for comparison. The positive charges on AuNP were introduced through surface modification with amine groups

DNA breaks were identified by monitoring changes in the plasmid conformation, and quantification was accomplished through agarose gel electrophoresis. We conducted a comparative analysis between positively (+) and negatively (-) charged AuNPs to study the effect of surface charge on dose enhancement.

Results and Discussion

The fraction of supercoiled DNA decreased with increasing radiation doses, indicating an increase in single-stranded breaks (SSBs). Figure 2 shows the fraction of the linear plasmid DNA exhibited dose-dependent increase, indicating the presence of double-stranded breaks (DSBs) (Fig. 2).

Lower concentrations of +AuNPs (approximately 200–3,000 times lower) than those used in cellular assays yielded a comparable degree of radiosensitization, generating both SSBs and DSBs. The dose enhancement factor (DEF) for +AuNPs was determined to be 1.3±0.2 and 1.5±0.4 for SSBs and DSBs, respectively, induced by photon beams [1,2]. However, SSBs and DSBs induced by carbon ions in the presence of +AuNPs and –AuNPs did not show significant differences. This observation may be attributed to the higher linear energy transfer (LET) associated with carbon ions than photon beams. Our ongoing research endeavors include incorporating additional data and exploring the effects of particle beams on varying LETs.
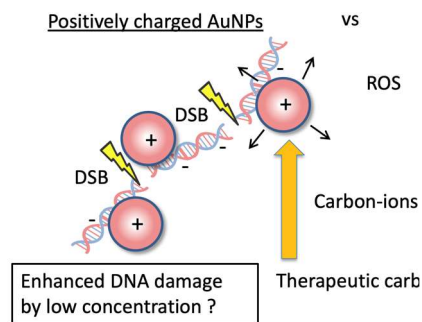
Fig. 1 Improving the microscopic dose enhancement factor using low +AuNPs concentrations via +AuNP–DNA binding for carbon-ion beams.
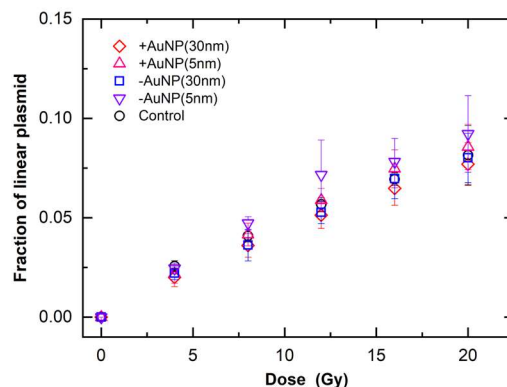

Fig. 2 Damage yields for plasmid DNA irradiated in the presence of AuNPs as a function of carbon-ion dose.

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Study on the Sewage Sludge Reduction and Solubilization Depending on Dose of Gamma Irradiation

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Introduction

Sewage sludge is a semi-solid slurry that can be produced as a by-product during sewage treatment processes. The accumulation of sewage sludge is continuously increasing, and the necessity for developing sludge reduction technologies also arises.

Sludge has a high moisture content, is large in volume, and contains pathogenic and hazardous substances, which poses a high environmental risk, so general treatment such as incineration and composting is limited. The Ministry of Environment is proposing anaerobic digestion-based sewage sludge reduction and biogas conversion technology as a unit process in the sewage treatment stage. Sludge solubilization technology is needed to increase the digestibility of sewage sludge and ensure highly efficient sludge reduction.

The gamma irradiation is suggested as a sludge solubilization technology that can destroy components such as sludge floc, EPS (Extracellular Polymeric Substances), and cell walls and convert sludge into highly biodegradable substrates [1,2]. The sludge reduction rate increases with gamma irradiation, by reducing the moisture content of sludge and the increasing biogas conversion rate. However, further research focusing on the optimization of this technology is needed. In order to enable the effective treatment of sludge, it is essential to assess the impact of doses.

In this study, we investigated the effect of radiation for sludge depending on doses ranging from 1.6 to 23.3 kGy. Shielding materials of aluminium, lead, and acrylic was manufactured with width calculation using Geant4 Monte Carlo simulation. The SCOD (Soluble Chemical Oxygen Demand), DTN (Dissolved Total Nitrogen), DTP (Dissolved Total Phosphorus), S-carbohydrate, and S-protein were measured to evaluate solubilization.

Materials & Methods

Shielding materials were manufactured to control the dose of sludge and composed of aluminum, lead, and acrylic considering the shielding rate. The thicknesses were determined with Geant4 MC simulation. Shielding materials were modeled on both sides of 6 cm of sludge and gamma irradiation was simulated in both directions. The source was defined for Co-60 emitting gamma of 1.17 and 1.33 MeV in a 1:1 ratio. Total number of primary particles produced in each simulation was 10^9.

The sludge used in this study was sourced from the Tancheon Sewage Treatment Plant, and the same sludge was used in all cases. Gamma irradiation was conducted at Greenpia, a Co-60 irradiation facility manufactured by Nordion. The sludge was irradiated at 14 dose points ranging from 1.6 kGy to 23.3 kGy depending on the dose.

The dose absorbed into each sludge was confirmed using alanine dosimeters, which could be used to measure doses from values in Gy up to hundreds of kGy. The alanine signals were analyzed by the ESR system which measures the numbers of free radicals produced by radiation interactions and converted into the doses by use of a calibration curve. Each alanine pellet was analyzed 10 times in the ESR system, and the dose was calculated as the average value, and the error per analysis was less than 3%.

The solubilization rate of sludge was evaluated using the SCOD analyzed according to standard procedures [3], and DTN, DTP, S-carbohydrate, and S-protein were also measured. The supernatants obtained by centrifuging the sludge at 10,000 rpm for 15 min were used to analyze the EPS. Carbohydrates and proteins were measured using the anthrone-sulfuric acid method, and the Lowry method, respectively [4].

The sludge solubilization rate was calculated with the coefficient of particulate COD release ratio ($P_{COD}RR$) using the following equation:

$$P_{cod}RR(\%) = \frac{SCOD_d - SCOD_0}{TCOD_0 - SCOD_0}100 \qquad (1)$$

where $SCOD_t$ is the amount of SCOD at dose d, $SCOD_0$ is the initial SCOD, and $TCOD_0$ is the total COD in the sludge.

Results and Discussions

The sludge was irradiated according to the dose and the changes in its properties had compared each other. The shielding materials were attached to both sides of sludge in accordance with the irradiation direction of the two-way irradiation facility. The dose irradiated to

the sludge was quantitatively measured using an alanine dosimeter.

DTN, DTP, S-carbohydrate, and S-protein for the gamma irradiated sludge were measured and compared with those for the control sludge in figure 1,2. Except for DTP, it showed an increase trend as the dose increased. The dose and amplitude of change were not completely proportional, but this can be accounted for within the standard deviation of the measurements. This alteration in chemical properties indicates the extent to which EPS, encompassing proteins, carbohydrates, DNA, and other compounds, underwent decomposition as the results of irradiation. DTP yielded results that were not significantly dose-related, indicating that additional pretreatment conditions were required to break phosphorus-related bonds.
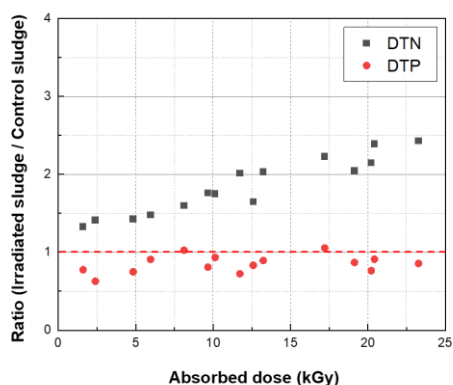

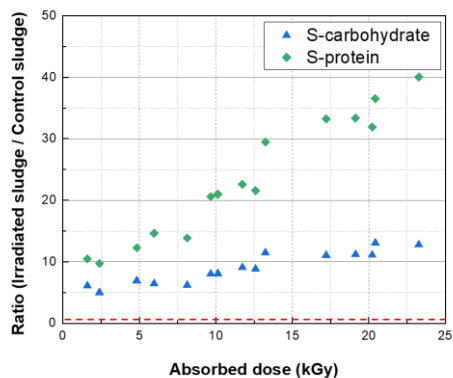Figure 1. Comparison of DTN and DTP between the gamma irradiated sludge and control sludge

Figure 2. Comparison of S-carbohydrate and S-protein between the gamma irradiated sludge and control sludge

The solubilization of irradiated sludge was calculated using equation (1) and is shown in Figure 3. $P_{COD}RRs$ are also large as the dose increased, and it is considered to be the comprehensive result of previously calculated evaluations. This solubilization result can also mean how much sludge has been reduced by breaking down the water content tightly bound to the EPS matrix.

Figure 3. The sludge solubilization rate depending on the dose
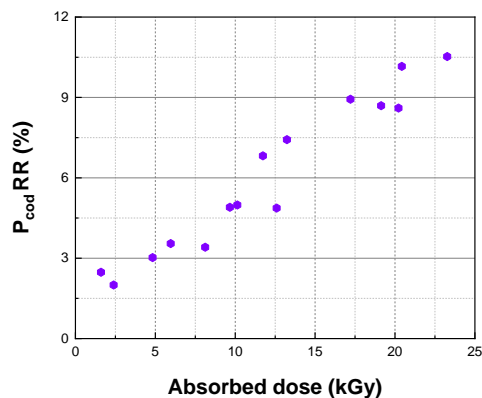
It was confirmed that irradiation can decompose non-decomposable substances, reduce the water content of sludge and reduce sludge. The study showed that the solubilization rate increased as the dose increased, and it is expected that dose optimization will be possible in more detail through the anaerobic digestion rate according to the dose.

Conclusion

In this study, we investigated the solubilization rate of sludge that varies depending on the dose in sludge treatment using radiation. The results of this study are expected to be useful in the development of sludge reduction technology using radiation.

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Simulation study of a bent crystal based monochromatic X-ray imaging with an X-ray tube

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Introduction

In synchrotron radiation experimental facilities, monochromatic X-rays are used for phase contrast imaging that utilizes quantification in objects. Monochromatic X-rays are obtained by diffracting white X-rays obtained from an accelerator under the Bragg condition using a Si monochromator. The beam size of synchrotron radiation X-rays is small due to their extremely high directivity, making it difficult to image large objects. Monochromation using such X-ray optics is possible because synchrotron radiation has high brilliance and directionality over a wide spectrum, while low-brilliance and divergent X-rays from an X-ray tube cannot provide a practical field of view or photon number.

To generate monochromatic X-rays with a large field of view from an X-ray tube, a method using a thin bent Laue-type Si single crystal was proposed by Zhong et al. in 1997 [1, 2]. Normally, when a flat Si single crystal is irradiated with X-rays, X-rays with monochromatic energy satisfying the Bragg condition diffract from the crystal, but when it is irradiated with divergent X-rays, a continuous X-ray spectrum diffracts from the crystal. If the crystal is bent to a fixed angle, X-rays in all directions can enter the crystal at the same angle of incidence to the crystal surface, and the same X-ray energy can be diffracted in all directions. This method is expected to provide a large monochromatic X-ray field of view, but it was first proposed and has not been put into practical use to date. It is difficult to curve thin crystals to the desired curves; in the setup of Zhong et al. The shape of the curve was calculated assuming that the light source was a point, but the focal spot size of the light source used was 0.3×1.0 mm^2, which is considered to cause a large loss of diffraction intensity.

Our research group has been developing an X-ray optical system made of thin Si single-crystals several tens of micro-meters thick for high image quality in refraction-contrast CT[3], and has the technology to set up and control thin crystals with high precision. If this technology is used for setting up bent Si single-crystals, it may be possible to generate a large, uniform field of view. In addition, the diffraction intensity can be increased by using a microfocus X-ray tube as a light source to diffract characteristic X-rays with a narrow spectral width and high brightness.

In this study, to investigate whether the Zhong et al. method can generate monochromatic X-rays that can be used for human imaging, the positional accuracy required to obtain a wide field of view with flat X-ray intensity and the number of X-ray photons generated under practical imaging conditions are obtained through simulations.

Methods

Figure 1 shows the geometry of X-ray monochromation using Laue-case bent Si single-crystals proposed by Zhong et al. The x-axis is set horizontally and the y-axis vertically to the light source. This figure illustrates only X-rays in a two-dimensional plane, but because the diffraction planes of the crystal are aligned perpendicular to the xy coordinate, similar diffraction occurs in the direction orthogonal to the xy coordinate. The radius of curvature between the X-ray beam and the crystal curve is defined by the following equation:

$$r(\theta) = R\exp(-\tan(\theta_B)\theta), \qquad (1)$$

where θ is the angle between the x-axis and the direction of the beam, R is the distance between the light source and the crystal surface when θ is 0 degree, and θ_B is the Bragg angle. Since the incident angle of all X-rays incident on this curve is θ_B, X-rays with a specific energy can be diffracted. X-ray beams incident on the diffraction plane of the crystal near the Bragg angle are divided into forward-diffraction beam and diffraction beam at the back of the crystal. These diffraction intensities follow a diffraction intensity curve that can be calculated theoretically from the X-ray energy and crystal lattice plane. To investigate whether the curvature condition in equation (1) can be used to obtain monochromatic X-rays that are practical for imaging, one-dimensional X-ray intensity profiles in the diffraction direction obtained at the back of a bent crystal are calculated by simulation. The simulation conditions are determined as follows.

1. X-ray tube

The energy of the monochromatic X-ray extracted from the energy spectrum of the X-ray tube is 17479 eV ($\Delta E \approx 5.77$ eV), which is the K$_{\alpha 1}$ ray of the characteristic X-ray of the Mo target. The focal spot size is set to 1 μm, assuming the use of a microfocus light source. The tube voltage, tube current, and exposure time are set to 50 kV, 1 mA, and 1 second, respectively. The anode angle is 12 degrees. The energy spectrum from the X-ray tube is obtained by using SpekPy, a toolkit that models an X-ray tube.

2. Laue-case bent Si single crystal

The diffraction plane used in the Laue-case bent Si single crystal is Si(111) with a thickness of 62 μm. The Bragg angle θ_B for the energy of the K$_{\alpha 1}$ ray is 5.6 degrees. The

Fig.1: X-ray Monochromation Geometry
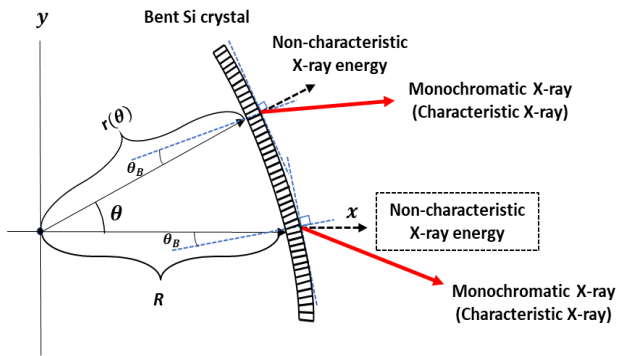
spectral width of the $K_{\alpha 1}$ ray and the intensity curve are taken into account when determining the diffraction intensity. The width of the diffracted beam produced at the back of the crystal is about 100 mm.

The pixel size for integrating the number of photons is 50×50 µm², assuming the pixel size of a medical X-ray system.

In the simulation, the following aspects will be investigated:
1. A fan-shaped X-ray beam generated by an X-ray tube is injected into a flat crystal to obtain the X-ray intensity profile in the diffraction direction. The number of photons produced in the diffraction direction is determined in this section. The number of photons of diffracted continuous X-rays other than characteristic X-rays, which can be a noise source, is also obtained simultaneously.

2. X-ray intensity profiles in the diffraction direction for bent crystals and the profiles when the light source is displaced in the x or y direction are obtained. Also, the acceptable amount of displacement should be checked.

Results
1. Diffraction intensity profile of plane crystal

The number of photons that can enter a 50×50 µm² pixel is about 220 photons per second for characteristic X-rays and about 0.35 photons per second for continuous X-rays. Although the number of photons is about three orders of magnitude lower than that of clinical X-ray systems, we believe that a practical number of photons can be obtained

by extending the exposure time. Continuous X-rays, which can be a source of noise, can be ignored because they are about three orders of magnitude smaller than characteristic X-rays.

2. Diffraction intensity profile of bent crystal

The diffraction intensity obtained with the bent crystal was about five times higher than that with the flat crystal. This is considered to be due to the fact that the same Bragg angle is satisfied in all directions by the curvature. The relationship between the amount of misalignment in the x- and y-directions and the intensity profiles show that the intensity changes more sensitively to misalignment in the y-direction. This result suggests that a misalignment of ±10 µm can be tolerated in the x-direction to obtain a uniform field of view, but in the y-direction, the position of the light source must be controlled to ±1 µm. The field of view is more than 10 cm by controlling the crystals and the light source in detail, and can cover the whole body of a human being.

Discussion

In this study, we reexamined the monochromatic X-ray generation method proposed by Zhong et al. and examined whether it is possible to generate monochromatic X-rays that can be used for human imaging. In the future, we will combine this monochromatic X-ray generation method with a phase-contrast imaging method and investigate a high-contrast imaging method using an X-ray tube.

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New Method for Dental Panoramic Reconstruction Using Cone-Beam Computed Tomography Projection Data

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Introduction

In dentistry, panoramic radiography and cone-beam computed tomography (CBCT) are vital for diagnosis and treatment planning. Panoramic radiography, while low in radiation and providing ample tooth information in 2D, and CBCT, offering highly detailed 3D data at a higher radiation dose, are essential tools. However, maintaining two separate systems is costly and space requirements. Software solutions have been explored to generate panoramic images from CBCT data. This approach allows you to acquire panoramic images without hardware modifications, but CBCT artifacts can affect image quality.

This study introduces a method to extract panoramic projection data from dental CBCT projection data. Leveraging the fact that CBCT covers panoramic scan trajectories, it identifies dental arches [1], determines a virtual panoramic scan trajectory, extracts the relevant data, and reconstructs the panoramic image. This method allows for an optimized focal plane, independent of the CBCT image, and is less affected by CBCT image quality, making it a promising approach in dental imaging.

Material and Methods

The proposed methodology comprises a series of key steps, as illustrated in Fig 1. These steps encompass.
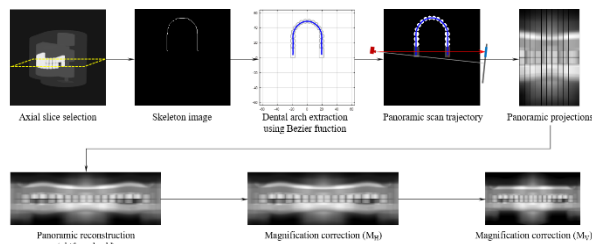

Fig. 1. Simplified process of the proposed dental panoramic reconstruction method

2.1. Dental Arch Detection

The CBCT image identifies dental arches, forming the foundation for panoramic scan trajectory. This paper introduces a method employing Bézier curves to detect teeth in CBCT images and establish the dental arch. To obtain the dental arch, an axial CBCT slice depicting overall tooth structure is selected through MIP. The MIP process accumulates row intensities, creating a graph. The MIP image is generated by determining top and bottom tooth positions based on a threshold within a certain range of the highest graph value. In the MIP image, teeth regions are segmented using a preset threshold, and a closing operation fills in lost regions. A skeleton curve, which represents the curve through the middle of the selected objects, is defined. To create a smooth panoramic image, Bézier curves, defined by control points, transform it into a differentiable continuous function:

$$B(t) = \sum_{i=0}^{n} \binom{n}{i} t^i (1-t)^{n-i} P_i$$

Here, t ranges from 0 to 1, and n specifies control points for Bézier curve optimization. The discrete skeleton curve is approximated as a continuous function through iterative control point adjustments to minimize differences between the two curves.

2.2. Panoramic Projection Acquisition

Following the acquisition of dental arch information, the panoramic scan trajectory in CBCT geometry is determined, mirroring the approach of conventional panoramic systems. This involves maintaining consistent source-to-object distance (SOD) and source-to-detector distance (SDD), with the dental arch acting as the object and the panoramic projection aligning with the dental arch direction. However, CBCT projections may exhibit varying magnification, necessitating correction. To address this, panoramic projections are obtained by dividing the optimized dental arch length into equal intervals. Each sampled dental arch segment's normal vector is calculated, a corresponding CBCT projection is selected, and cropping is performed to derive a panoramic projection. The length of the panoramic projection matches that of the sampled dental arch. This process is repeated for all sampled dental arch segments to generate panoramic projections.

2.3. Panoramic reconstruction & magnification correction

The panoramic projection data obtained is utilized to reconstruct the panoramic image. This reconstruction utilizes the shift-and-add method [2] with auto-focusing. The width of the focal plane from which the panoramic image is derived depends on the extent of shift applied in the shift-and-add method. As the shift amount varies, the focal plane width adjusts accordingly, akin to a tomosynthesis image. Since the panoramic projections obtained from CBCT geometry exhibit varying magnification, they may introduce distortion during image reconstruction. To rectify this,

magnification correction is applied. The magnification of each panoramic projection is adjusted sequentially for both vertical (M_V) and horizontal (M_H) dimensions to align with a reference projection's magnification. This iterative process culminates in the creation of the final corrected panoramic image.

The proposed method integrates dental arch detection, panoramic projection acquisition, and panoramic image reconstruction with magnification correction. It addresses the challenges posed by varying magnifications in CBCT geometry, ensuring the production of high-quality panoramic images tailored to individual patient characteristics.

Table. 1: Parameter used in simulation

Parameter	Dimension
No. of projection	720
Voxel dimension	$512 \times 512 \times 512$
Voxel size	1.0 (*mm*)
Pixel dimension	1268×276
Pixel size	0.8 (*mm*)
Source-to-object distance	362.0 (*mm*)
Source-to-detector distance	724.1 (*mm*)

Results and Discussion

3.1. Dental arch phantom

To validate proposed algorithm using a numerical dental arch phantom. The dental arch phantom used in the simulation consisted of a tooth, the spine, and soft tissue, with a few missing teeth in the mandible. Fig 2 (a) shows a panoramic image reconstructed using panoramic projections obtained from the CBCT projection data. The magnification of each panoramic projection is not the same, resulting in a distortion of the panoramic image. Finally, a distortion-free panoramic image was obtained by applying vertical and horizontal magnitude corrections. To compare the image quality of the panoramic images reconstructed using the proposed algorithm, we compared it to a panoramic image acquired using a conventional panoramic scan trajectory.
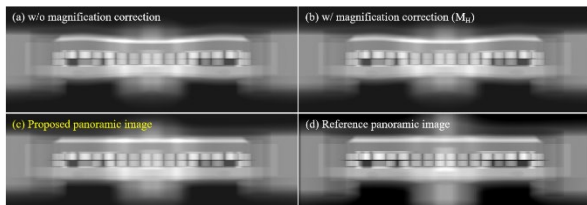

Fig. 2. Simplified process of the proposed dental panoramic reconstruction method: (a) specifying patient's dental arch from the CBCT image, (b) extracting panoramic projection data from the CBCT projection data, (c) reconstructing a panoramic image, and (d) correcting image magnification.

3.2. Real bone phantom

To verify the performance of the proposed algorithm in a real-world environment, we conducted experiments using a real bone phantom. The phantom used in the experiment is a real bone phantom made from real human bones and teeth. Compared with a typical head phantom, the real bone phantom makes it possible to obtain radiographs of the same teeth and bones as in a clinical case. The dental arch detection algorithm using Bézier function optimization performed well on the experimental data. The panoramic images reconstructed from the CBCT projection showed good image quality.
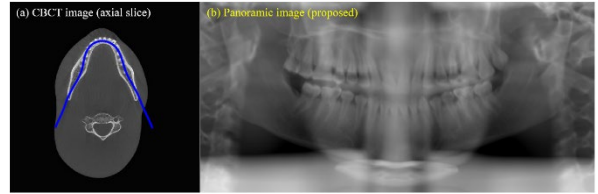

Fig. 3. Experimental results: (a) dental arch extracted through Bézier curve, and (b) proposed panoramic image reconstructed using the CBCT projection data before applying an appropriate image enhancement process.

Conclusion

In this study, we propose an effective method for reconstructing a panoramic image by extracting panoramic projection data from dental CBCT projection data, thereby eliminating the need for an additional panoramic scan. This method involves patient-adaptive dental arch detection using CBCT projection data and (SAA) based panoramic reconstruction through the acquisition of a panoramic projection. The image quality of the proposed panoramic image, based on CBCT projection, is comparable to that of conventional panoramic images. The introduction of this method is expected to assist dental clinics in performing various procedures by enabling the acquisition of panoramic images without requiring further modifications to the hardware of existing dental CBCT equipment.

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Department sessions

				Biomedical Laboratory Science/Medical Technology
13:30-13:40	Opening remarks	Prof. Mitsuo Sato	Nagoya	
Session I				
	Chair	Prof. Tetsuya Ishikawa	Nagoya	
13:40-14:00		Miyu Isogai	Nagoya	Molecular characterization of three closely related species of Klebsiella pneumoniae (K. pneumoniae, K. quasipneumoniae, and K. variicola)
14:00-14:20		Jin Han	Yonsei	Identification of Colorectal Cancer-related Biomarkers from Whole Blood using Integrated Bioinformatics Analysis
14:20-14:40		Chiharu Yamada	Nagoya	ZNF384-fusion proteins upregulate RGS1, which may attenuate CXCL12-CXCR4 signaling
	Intermission (15 min)			
Session II				
	Chair	Prof. Jung-Yoon Yoo	Nagoya	
14:55-15:15		Jin-Seok Jung	Yonsei	Identification of Molecular Mechanisms in the pathogenesis and development of Liver Fibrosis
15:15-15:35		Nanami Yoshida	Nagoya	Quercetin prefers to induce the expression of type 3 inflammatory chemokine CXCL2 in macrophages
Session III				
	Chair	Prof. Tsutomu Kawabe	Nagoya	
15:35-15:55		Woo-Seung Kim	Yonsei	Identification of Regulatory Mechanisms of Colonic pH in Enterotoxigenic Bacteroides fragilis Toxin Secretion

15:55-16:15		Fuzuki Hayashi	Nagoya	Analysis of immune responses in NC/Nga mice focusing on lymphocytes
16:15	Closing remarks	Prof. Fumihiko Hayakawa	Nagoya	
16:25	Commemorative photographing			

Molecular characterization of three closely related species of *Klebsiella pneumoniae* (*K. pneumoniae*, *K. quasipneumoniae*, and *K. variicola*)

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Introduction

Klebsiella pneumoniae is a Gram-negative bacterium belonging to the order *Enterobacterales*, which is commonly found in the human intestines and respiratory tract. It is considered an opportunistic pathogen, primarily causing urinary tract infections, respiratory infections, bloodstream infections, and liver abscesses, especially in immunocompromised individuals. In the medical environment, *K. pneumoniae* has shown a trend towards multidrug resistance due to daily exposure to antibiotics. The World Health Organization is concerned about the increasing prevalence of strains producing extended-spectrum β-lactamase (ESBL) and carbapenem-resistant strains (Carbapenem-resistant *K. pneumoniae*, CRKp), as well as the high mortality rate associated with infections caused by this bacterium [1]. Additionally, reports of outbreaks of highly virulent hypervirulent *K. pneumoniae* (HvKp) with high viscosity have emerged in Asian regions, including Taiwan [2], and their trends are being closely monitored in Japan.

Advancements in the study with whole-genome sequencing (WGS) in recent years have revealed that clinical strains identified as *K. pneumoniae* include not only *K. pneumoniae* but also closely related species such as *K. quasipneumoniae* and *K. variicola* [3]. *K. quasipneumoniae* has been reported to acquire drug-resistance plasmids from environmental bacteria and transfer them to other *Enterobacterales*, acting as a vector [4]. *K. variicola*, on the other hand, exhibits higher pathogenicity and tends to have a higher mortality rate from bloodstream infections compared to *K. pneumoniae* [5]. While the importance of these non-*K. pneumoniae* species is becoming increasingly evident, research on these species is scarce in our country, and routine hospital diagnostics have yet to classify these three closely related species.

Therefore, this study aims to elucidate the frequency and molecular biological characteristics of *K. pneumoniae*, *K. quasipneumoniae*, and *K. variicola*.

Materials and Methods

Bacterial strains and culture conditions

A total of 269 clinical strains collected from January 2015 and Jun 2021 at Nagoya University Hospital, located in Japan. All these strains were obtained from blood cultures and initially identified as *K. pneumoniae* or *K. variicola* using matrix-assisted laser desorption ionization-time-of-flight mass spectrometry (MALDI-TOF/MS). All strains were stored at -80 °C before use.

Sequencing reads of the clinical strains are available under the BioProject accession numbers PRJDB14656.

WGS and assembly

Illumina short-read sequencing was performed on the 269 strains. Genomic DNA was extracted using the Gentra Puregene Yeast/Bact.Kit (Qiagen, Germany) then DNA concentrations were quantitated with the Quantus FLUOROMETER (Promega, WI). Sequencing libraries were prepared using QIAseq FX DNA Library kit (Qiagen, Germany) according to the manufacturers' instructions, and the libraries were sequenced with Illumina NextSeq 2000 sequencer using NextSeq 1000/2000 P2 Reagents (300 cycle). Low-quality raw reads were trimmed using fastp and assembled by SPAdes version 3.13.1.

Identification of species

The species of 269 strains were determined using OrthoANI based on the WGS data [6,7]. The reference genomes were *K. pneumoniae* HS11286 (PRJNA78789), *K. quasipneumoniae* KqPF26 (PRJNA683049), and *K. variicola* LEMB11 (PRJNA541977). The cut-off values of average nucleotide identity (ANI) for the identification of bacterial species were set at 95%.

Identification of genotypes

Antimicrobial resistance genes (with 90% identity and 60% minimum length) were identified by the AMRFinderPlus-3.11 version 3.11.18.

Virulence genes (with 90% identity and 60% minimum length) and capsular genotypes were

identified using BLASTn according to the online database of the Pasteur Institute MLST for *K. pneumoniae*.

Results and discussion

Ratio of K. pneumoniae, K. quasipneumoniae, and K. variicola

First, we identified the isolation ratios among 269 clinical isolates. The 269 isolates were identified as follows: *K. pneumoniae* 6% (n=190, 70.6%), *K. quasipneumoniae* (n=32, 11.9%), and *K. variicola* (n=47, 17.5%). This distribution aligns with the results reported by Imai *et al.* [8], implying that approximately 30% of *K. pneumoniae* isolates in Japan may potentially belong to *K. quasipneumoniae* and *K. variicola*.

Antimicrobial resistance genes

We confirmed the presence of β-lactamase genes, including chromosomal genes, as an indicator of antimicrobial resistance. Eight distinct of β-lactamase genes were identified among *K. pneumoniae* strains, four were identified among *K. quasipneumoniae* strains, and only two were detected among *K. variicola* strains. Among these ESBL genes were observed in 38 out of 190 *K. pneumoniae* strains (20.0%) and 2 out of 32 *K. quasipneumoniae* strains (6.3%), but were absent in *K. variicola* strains. Regarding carbapenemase genes, they were detected in only 2 out of 190 *K. pneumoniae* strains (1.1%), while no presence observed in *K. quasipneumoniae* or *K. variicola* strains. Previous research has highlighted the role of antimicrobial resistance plasmids in *K. quasipneumoniae* in facilitating gene transfer and plasmid rearrangement within the hospital environment [4]. However, in this study, relatively limited number of antimicrobial resistance genes were observed among *K. quasipneumoniae* strains.

Virulence genes

We identified the K1 and K2 capsular genotypes commonly associated with highly virulence strains and verified the presence of genes related to virulence, including capsule production, iron carrier, and type 3 pili. Strains exhibiting the K1 and K2 capsular genotypes, were observed in 7 strains (3.7%) and 1 strain (0.5%) of *K. pneumoniae* respectively, but were not found in any *K. quasipneumoniae* or *K. variicola* strains. Regarding virulence genes, *K. pneumoniae* was found to harbor 21 distinct genes, while *K. quasipneumoniae* possessed 12, and *K.variicola* exhibited only 3. Although there have been reports suggesting a high pathogenicity of *K. variicola* [5], in this study, *K. variicola* had a relatively limited number of virulence genes.

Conclusions

About 30% of *K. pneumoniae* clinical isolates in Japan could be *K. quasipneumoniae* or *K. variicola*, which have fewer resistance and virulence genes than *K. pneumoniae*. It is reported that *K. quasipneumoniae* is associated with colonization, while *K. variicola* has a higher 30-day mortality rate [9]. Therefore, distinguishing these species and analyzing their genes is crucial for understanding *Klebsiella* species.

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Identification of Colorectal Cancer-related Biomarkers from Whole Blood using Integrated Bioinformatics Analysis

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Introduction

The gene expression Omnibus (GEO) database is a comprehensive resource for gene expression data generated by numerous technologies, such as microarrays, next-generation sequencing, and other high-throughput methods. Researchers from around the globe can submit their gene expression data to GEO, making it accessible for further analysis and investigation by the scientific community. By providing a centralized repository for gene expression data, researchers are able to compare their own findings with existing datasets to discover new insights.

In addition, Human Transcription Factors (TF) Database, expression quantitative trait loci (eQTL) Gene Consortium, disease Gene Search Engine (DigSeE) database, and Colon Rectal Cancer Gene Database (CoReCG) database can also provide a wealth of cancer-related data.

In this study, we used Korean whole blood samples and the above databases for obtaining novel markers associated with colorectal cancer.

Materials and Methods

a. Retrieval of Blood Genome-Wide Transcriptomic Datasets

Peripheral blood gene expression datasets were retrieved from the Gene Expression Omnibus (GEO) database.

b. Protein-Protein Interaction network analysis

The String App plugin (version 1.6.0) in Cytoscape (version 3.8.2) was used to load the protein-protein interaction (PPI) network from the Search tool for the retrieval of integrating genes/proteins (STRING, https://string-db.org). A PPI network of DEGs from RNA sequencing analysis was constructed. And Network Analyzer plugin (version 4.4.6) in Cytoscape (version 3.8.2) was applied to evaluate the degree of interaction between nodes of the PPI network.

c. Composing Korean CRC-related whole blood (KCRWB) dataset through RNA sequencing analysis and differentially expressed gene (DEG) analysis

RNA sequencing analysis and DEG analysis were requested at Macrogen in Seoul, Republic of Korea, with 10 samples from each group to explore novel RNA biomarkers in Koreans. Samples were analyzed using Agilent 2200 Tape Station System (Agilent Technologies, CA, USA) to assess the integrity of total RNA. Only high-quality RNA samples with RNA integrity number (RIN) greater than 7.0, were used for RNA library construction. The DESeq2 package in the R software was used to identify DEGs between each group. DESeq2 analyzes read-count data from RNA sequencing as one of the representative methods of DEG analysis.

d. Statistical analysis

Statistical analysis was performed using the software packages PRISM version 7.01 (GraphPad Software, CA, USA) and 2022 Minitab 21.3 (Minitab Inc, Barbara F. Ryan Penn, USA). Student's t-test was performed to determine the statistical significance of differences between groups. p-value < 0.05 were considered statistically significant.

e. RT-qPCR method

Complementary DNA (cDNA) was synthesized using an M-MLV reverse transcriptase (Invitrogen, CA, USA), random hexamers (Invitrogen), and dNTP mixture (Intron Biotechnology, Seongnam, Republic of Korea) according to the manufacturer's recommendations. The expression of each gene relative to that of glyceraldehyde-3-phosphate dehydrogenase (GAPDH) gene was measured by quantitative polymerase chain reaction (qPCR) using TaqMan probes in a CFX-96 real-time PCR system (Bio-Rad Laboratories, CA, USA).

Results

a. Selection of the GEO dataset and pre-processing of the dataset

Peripheral blood gene expression datasets were retrieved from the GEO database by searching with the keywords 'Colorectal cancer' and 'Human whole blood'. By manual inspection based on two criteria: (1) transcriptome data from whole blood samples and (2) availability of comparisons between CRC patients before any treatment and healthy controls, GSE164191 and GSE11545 datasets satisfying the above criteria were used to identify CRC-related genes.

b. Protein-Protein Interaction network analysis for GEO datasets

Compare with these two datasets of GSE164191 and GSE11545 there were 8,966 common genes. Subsequently, genes with p-value <0.05 and fold-change more than 1.5 times between CRC group and control group were determined to be DEGs. This selection process resulted in a reduced collection of 956 genes.

We mapped 956 DEGs onto the PPI network and 166 genes were selected as the DEG$_{Hub}$ dataset with more than 10 interactions.

c. Identification of Blood CRC-related Genes using five publicly available datasets (PADs)

As a result of performing an intersection analysis between 956 DEGs from the GEO dataset and transcripts from five PADs respectively, each PADs' intersection results were obtained. (Table 1)

Table. 1.The union results of GEO database and five PADs.

No.	GEO - PADs	Upregulated transcripts	Downregulated transcripts	Total transcripts
1	GEO - Hub	45	87	132
2	GEO - DiGSeE	21	27	48
3	GEO - TF	24	103	127
4	GEO - eQTL	43	151	194
5	GEO - CoReCG	33	64	97

d. Selection of candidate genes for clinical validation

An intersection analysis between the PAD datasets and the KCRWB dataset was conducted. There exists a group of seven circulating transcripts that are shared between two datasets: *ADAMTS1, DLG5, NQO2, CD177, SH2D1B, KRT73, and SLC26A8*. To further filtrate candidates, the expression tendency of seven genes was investigated. (Figure 1)

Figure 1. The scatter plot of expression tendency of seven circulating transcripts
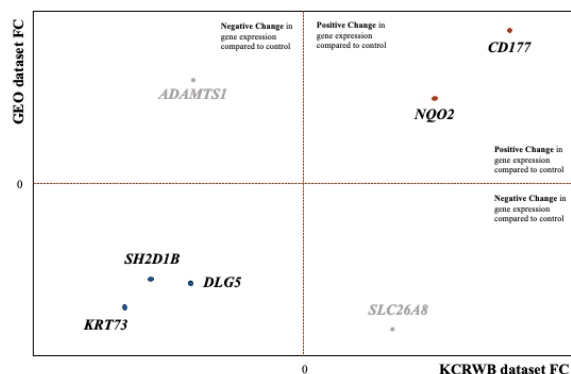

an X-axis was a fold change value for the KCRWB dataset, and a Y-axis was a fold change value for the GEO dataset. The middle of the center in the X and Y-axis was the zero point, and the standard of zero point divided both sides as negative change and positive change in gene expression compared to the control group.

Accordingly, five circulating transcripts (*DLG5, NQO2, CD177, SH2D1B, KRT73)* that exhibit same expressions when compared to the GEO and KCRWB dataset were chosen as a set of genes for clinical validation.

e. Clinical validation for five circulating transcripts with reverse transcription quantitative polymerase chain reaction (RT-qPCR)

A total of 106 samples from the colorectal cancer (CRC) group and 123 samples from the healthy control (HC) group were utilized for the RT-qPCR analysis. The *DLG5, CD177, SH2D1B, and NQO2* exhibited statistical significantly increased results in the t-test analysis. The expression of *KRT73* was found to be decreased in the colorectal cancer (CRC) group. But the statistical analysis conducted using a t-test did not yield significant results for the *KRT73* variable (Figure 2).

Figure 2. The clinical validation results of five circulating transcripts
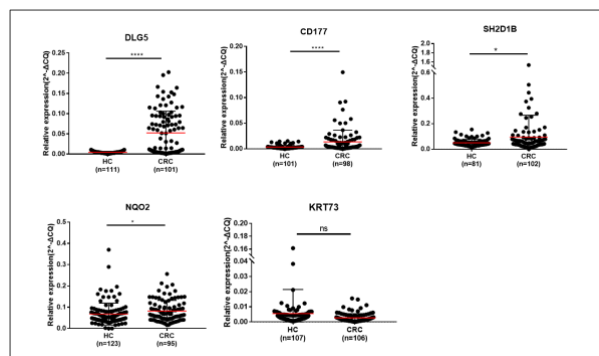
Discussion

According to the Clinical validation results, at least four of these five circulating transcripts could be useful as diagnostic markers for colorectal cancer. In addition, we can infer that the method used to investigate biomarkers for colorectal cancer with PADs was a valuable one because it incorporated multiple environmental and genetic datasets.

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ZNF384-fusion proteins upregulate RGS1, which may attenuate CXCL12-CXCR4 signaling

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Introduction

B-cell acute lymphoblastic leukemia (B-ALL) is a hematological malignancy frequent in children and elderly, and is caused by the clonal proliferation of B-lymphoid progenitor cells [1]. Recurrent cytogenetic and molecular abnormalities have been shown to play key roles in the pathogenesis of B-ALL.

ZNF384 fusion (Z-fusion) genes are recently identified in B-cell acute lymphoblastic leukemia (B-ALL) and characteristically frequent in Asian adult patients. The frequency is about 20% in Philadelphia chromosome negative B-ALL. Several fusion partners such as TCF3 and TAF15 are identified and whole ZNF384 are fused to the C-terminal sides of the fusion partner proteins in Z-fusion proteins (fig.1). Z-fusion proteins are expected to be gain-of-function mutants of ZNF384, a transcription factor. We and others demonstrated the development of leukemia by introducing a Z-fusion gene into mouse hematopoietic cells, strongly indicating its leukemogenicity [2]; however, detailed mechanisms of leukemogenesis by Z-fusion proteins have yet to be clarified.

In the present study, we searched the transcriptional targets of Z-fusion proteins by analyzing the gene expression profiles of Z-fusion gene transfected cell lines and clinical ALL samples. And, we did a functional analysis of these transcriptional targets.
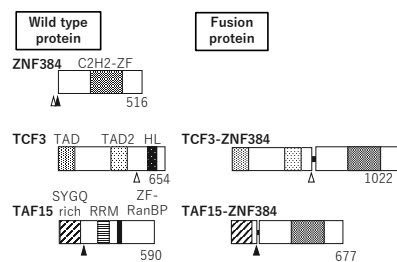

fig1. structures of Z-fusion proteins

Method

We established two cell lines expressing TCF3-ZNF384 (TCF3-Z) or TAF15-ZNF384 (TAF15-Z), performed RNA-seq, and analyzed differentially expressed genes (DEG) due to Z-fusion protein expression. We also analyzed DEG between *Z-fusion gene*-positive and negative ALL using the previous RNA-seq data of 323 Japanese ALL patients. We searched the direct transcriptional targets of Z-fusion proteins using both DEG data and ChIP-seq data obtained from ENCODE data base. Then, we investigated the binding of Z-fusion proteins to the regulatory regions of the candidate genes by ChIP-qPCR. Finally, we tested the effects of the candidates on cell proliferation and chemokine chemotaxis.

Results

We searched the direct transcriptional targets of Z-fusion proteins using two DEG data. 272 genes were upregulated by Z-fusion protein expression in LCL trasnfectant and 187 genes showed higher expression in *Z-fusion gene*-positive ALL than negative one. Out of 26 commonly upregulated genes, we selected 6 genes to which ZNF384 strongly bound using ChIP-seq data. The candidate genes were, *CREB5*, *RGS1*, *RIN3*, *PLEKHG1*, *CHST12* and *TESK2* (fig2).
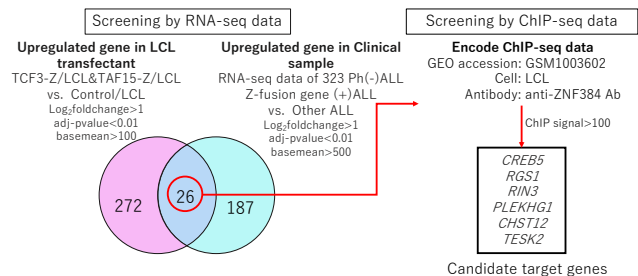

fig2. Seatch of transcriptional target genes

We examined the expressions of the candidate genes by RT-qPCR. The expressions of all genes were significantly higher in Z-fusion-expressing LCL than Control LCL. We performed ChIP-qPCR to examine the binding of Z-fusion proteins to these genes in LCL transfectants. TCF3-Z bound to all the target genes, while TAF15-Z associated with only *CREB5* and *RGS1*
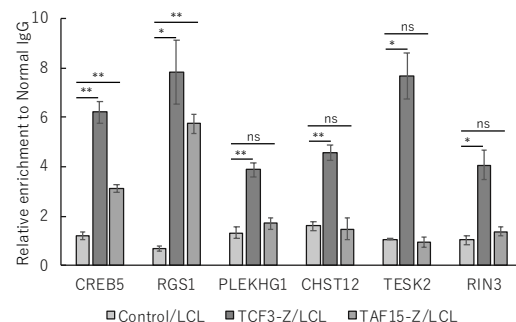

fig3. Binding of Z-fusion proteins to candidate genes in LCL transfectants

(fig3), indicating that *CREB5* and *RGS1* were the common direct targets of Z-fusion proteins.

We examined the effect of the expression of CREB5 and RGS1 on the survival of Z-fusion gene-positive ALL cell line, JIH5, by knock down experiments; however, Neither knock down of CREB5 nor RGS1 affected the survival of JIH5 (data not shown).

RGS1 is an inhibitor of CXCR4 signaling and it is reported that overexpression of RGS1 in pro B cell impaired CXCL12-induced chemotaxis [3]. We examined CXCL12-induced chemotaxis of TCF3-Z/LCL by transwell assay. CXCL12-induced chemotaxis was impaired in TCF3-Z/LCL, suggesting that TCF3-Z induced RGS1 expression attenuate CXCL12-induced chemotaxis (fig4).
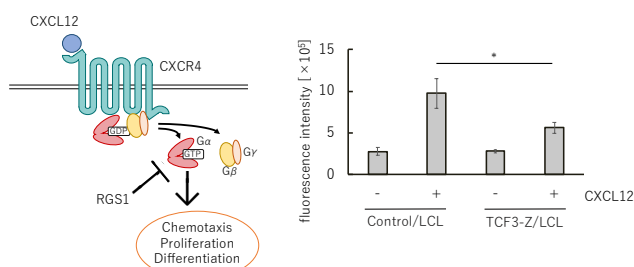

fig4. CXCL12-induced chemotaxis was impaired in TCF3-Z/LCL

Discussion

Two methods have been reported to search transcriptional targets of Z-fusion proteins. The one was selecting genes upregulated by the transduction of *EP300-Z* gene to cell lines [4], and the other was picking up DEG between Z-fusion gene-positive and negative ALL samples [5]. These methods were insufficient because the genes upregulated in cell lines might not be expressed in primary ALL cells and the genes highly expressed in Z-fusion gene-positive ALL might not be regulated by Z-fusion proteins. In the present study, we used both approach to screen the transcriptional targets of Z-fusion proteins.

CXCL12 is thought to play important roles in retaining early B cells in bone marrow microenvironment and supporting B cell differentiation through CXCL12-CXCR4 signaling. It is reported that targeted disruption of the CXCL12 gene is accompanied by defects in B cell lymphopoiesis [6]. These findings raises a possibility that RGS1 high expression induced by Z-fusion proteins impairs B cell differentiation through inhibiting CXCL12-CXCR4 signaling.

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Identification of Molecular Mechanisms in the pathogenesis and development of Liver Fibrosis

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Introduction

Liver fibrosis is a pathological condition characterized by the abnormal accumulation of extracellular matrix (ECM) due to chronic liver disease, representing a significant global health challenge [1]. There is a significant unmet medical need for anti-fibrotic therapies to prevent hepatic disease progression, however, there is currently no approved therapy for liver fibrosis.

Elucidating the molecular mechanisms underlying the amelioration of liver fibrosis is of paramount significance. Recent studies have reported that epigenetic dysregulation is a common factor in the progression of human diseases, including fibrosis [2]. However, the precise mechanisms underlying these processes still require further elucidation.

In this study, we have elucidated the significance of the molecular mechanism mediated by p300, a histone acetyltransferase, in the progression of liver fibrosis. Furthermore, we aim to elucidate another molecular mechanism underlying liver fibrosis by employing these experimental techniques.

Methods

Mouse Experiments

All animal experiments were approved by Yonsei University College of Medicine Institutional Animal Care and Use Committee (IACUC No. 2019-0313).

C57BL/6 mouse group was fed a choline-deficient, L-amino acid-defined, high-fat diet (CD-HFD) for 4 weeks to inducing liver fibrosis. Inhibitors were administered 3 times/weeks.

LX-2 cell culture

To induce fibrosis in vitro, LX-2 cells, human hepatic stellate cells, were initially subjected to a 2-hour period of serum starvation and subsequently stimulated with 20 ng/ml of TGF-β1. Various inhibitors were co-treated with TGF-β1, and and cell harvesting was performed after 24 hours.

Western blot assay

Protein samples were prepared from cells and tissues by lysis. Protein samples were separated and transferred to PVDF membranes. Primary and secondary antibodies were attached to membranes, and chemiluminescence signals were visualized using the Fusion SOLO S device.

RNA isolation and quantitative reverse transcription-polymerase chain reaction (qRT-PCR) analysis

Total RNA was extracted from fresh liver tissues and LX2 cell lines. Subsequently, qRT-PCR analyses were conducted, with target gene expression levels normalized by comparison to GAPDH expression levels.

Liver histopathological staining

Mouse livers were isolated under anesthesia and fixed by formalin. After fixation, liver tissue was embedded in paraffin and sectioned. Liver sections were de-paraffinized with xylene and rehydrated through 100%, 90%, and 80% ethyl alcohol series prior to staining(Masson's trichrome staining (MTS), Sirius red staining, Immunohistochemical staining (IHC).

Results

We investigated regression of liver fibrosis in mice induced by Choline-Deficient, High-Fat Diet (CD-HFD) using p300-specific inhibitors, A6 and C646 (Fig 1A) [3]. CD-HFD mice induced liver fibrosis displayed elevated p300 protein levels (Fig. 1 B, D). However, treatment with p300-specific inhibitors resulted in a significant improvement in histological features (Fig. 1B, C). Western blot analysis further revealed decreased levels of p300, αSMA (alpha-smooth muscle actin), and COL1A (collagen type 1A) proteins in the liver tissues treated with p300 inhibitors (Fig. 1D). The reduction of fibrosis after treatment with p300 inhibitors was also observed in mRNA levels of fibrosis marker genes,
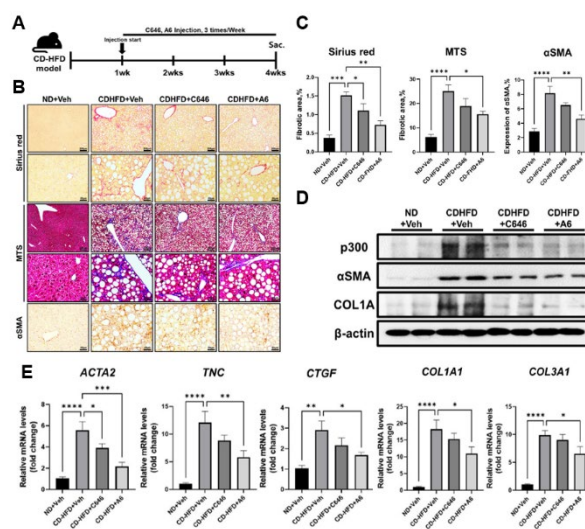

Figure 1. Amelioration of CD-HFD-induced liver fibrosis by p300 inhibitors.
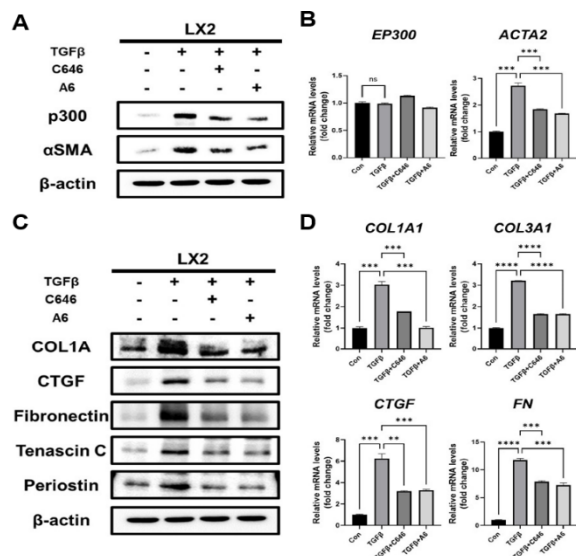
Figure 2. Suppression of pro-fibrotic responses in TGF-β1-stimulated LX2 cells via disruption by p300 inhibitor.

actin alpha 2, αSMA (ACTA2), tnascin C (TNC), connective tissue growth factor (CTGF) and collagen type 1, alpha 1(COL1A1) and collagen type 3, alpha 1(COL3A1) (Fig. 1E).

To elucidate the molecular mechanism of liver fibrosis at the cellular level, we utilized human hepatic stellate cells (LX2) treating TGF-β. Stimulation with TGF-β1 increased αSMA expression levels in LX2 cells, which were significantly reduced by p300 inhibitors (Fig. 2A, B). Furthermore, treatment with p300 inhibitors following TGF-β1-induced fibrosis ameliorated the elevated expression of fibrosis markers, including COL1A, CTGF, fibronectin (FN), TNC, and periostin induced by TGF-β1 (Fig. 2C, D).

Discussions

Liver fibrosis is life-threatening disease worldwide [1]. There are no approve drugs for the treatment of liver fibrosis, therefore, it is crucial to elucidate the molecular mechanisms of liver fibrosis to propose therapeutic strategies.

In this study, we demonstrated that molecular mechanism of in liver fibrosis via p300, analyzing expression levels of fibrotic marker in CD-HFD mouse model and TGF-β induced hepatic stellate cells (HSCs) model. The CD-HFD mouse model was designed to enhance lipid uptake while diminishing their release in liver, thereby inducing the development of liver fibrosis through Non-Alcoholic Steatohepatitis (NASH) [4]. HSCs are myofibroblast progenitor cells in the liver and key effector cells in liver fibrogenesis and fibrosis progression [1]. HSCs induced by TGF-β are driving liver fibrosis. These

experimental tools had facilitated the elucidating molecular mechanism that p300 inhibition alleviated liver fibrosis suppressing HSCs activation.

Based on these techniques, we aim to investigate another molecular machanism in liver fibrosis. We selected inhibitors affecting differnt molecular machanisms and analyzed effects of fibrotic progression in TGF-β induced LX2 cell. some inhibitors appeared to regulate the fibrotic progression (Fig. 3).

In future study, we intend to verify whether these inhibitors and target molecules regulate fibrosis and how they regulate the molecular mechanisms of liver fibrosis utilizing above experimental tools.
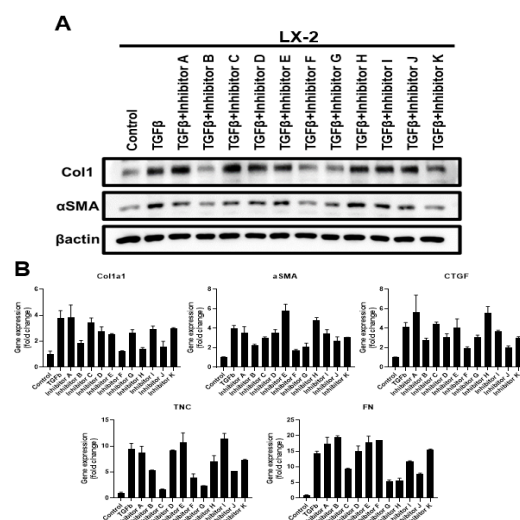

Figure 3. Effects of candidate inhibitors on Fibrotic Progression in TGF-β-Induced LX2 Cells.

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Quercetin prefers to induce the expression of type 3 inflammatory chemokine CXCL2 in macrophages.

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Introduction

Flavonoids are organic compounds found in natural plants. Quercetin is one of the flavonoids found abundantly in fruits and vegetables. We have previously reported that quercetin has various cytoprotective effects, including anti-allergic, anti-inflammatory, and anti-oxidative effects via nuclear factor E3 related factor 2 (Nrf2)-heme oxygenase (HO)-1 pathway [1, 2, 3]. Nrf2 is one of the stress-sensing transcription factors and has an important role in cellular defence [4].

Immune responses are classified into three different types depending on the species of pathogens, and the type of effector T-cell and innate lymphoid cell (ILC) lineages [5, 6]. Type 1 response protects against intracellular pathogens through activation of Th1 cells, CD8+ cytotoxic T cells, ILC1, and natural killer cells. Type 2 response induces the activation of Th2 cells and ILC2 against helminths and venoms. Type 3 response targets extracellular bacteria and fungi, and Th17 cells and ILC3 perform significant functions in this response. During these immune responses, chemokine produced by stromal and inflammatory cells promote the recruitment of polarized T cells and specific effector cells at the local site of inflammation.

Although quercetin suppressed the production of inflammatory cytokines, such as TNF-α, IL-1β, and IL-6, induced by various stimuli, we found that quercetin induced the expression of CXCL2 (macrophage inflammatory protein-2, MIP-2), which triggered neutrophil chemotaxis in a type 3 immune response. However, it is unclear how quercetin regulates chemokine expression and how it works on cells.

In this study, we investigated the effects of quercetin on chemokine expression acting on type 1, type 2, and type 3 immune responses.

Materials and Methods

Cell culture

RAW264.7 cells were cultured in RPMI1640 culture media containing 10% fetal bovine serum, 100 U/ml penicillin, 0.1 U/ml streptomycin, 2.5 x 10^{-4} U/ml amphotericin B, and 1 mM sodium pyruvate at 37°C under humidified 5% CO_2 conditions.

Establishment of HO-1 knock out (KO) RAW264.7 cells by CRISPR/Cas 9 system

Two types of sgRNAs that recognized different sites in the HO-1 gene sequence were used. Target-complementary CRISPR RNA (crRNA) (100 μM) and trans-activating crRNA (tracrRNA) (100 μM), were mixed with equal amounts (final concentration 50 μM), and then heated at 95 °C for 5 min. The temperature was slowly lowered to 25 °C to synthesize sgRNA. The RNP complexes were synthesized by mixing the respective sgRNAs with Cas 9 enzyme (New England BioLabs, MA, USA) in a 2:1 ratio and incubated at room temperature for 20 min. RAW264.7 cells (1.4 x10^4 cells/μl) were reacted on ice for 5 min, and then 15 μl each of the two RNP complexes were added. The cells were then transferred to a 2 mm wide cuvette and electroporated (Bio Rad Laboratories) at 250 V, 500 μF. After electroporation, the cells were transferred to a 6-well plate and incubated at 37 °C, 5% CO_2 for 72 h. Single cell clones were isolated by limiting dilution using a 96-well plate.

Quantitative real-time polymerase chain reaction

Total RNA was extracted from cells by using ISOGEN II (Nippon Gene, Toyama, Japan) or RNAiso Plus (Takara Bio, Shiga, Japan) and transcribed into cDNA by PrimeScript RT reagent kit (Takara Bio) or ReverTra Ace® qPCR RT Master Mix (Toyobo, Osaka, Japan). Quantitative real-time PCR was performed on a Thermal Cycler Dice Real Time System II (Takara Bio). The expression levels of each target gene were normalized with an endogenous reference gene (*Gapdh* or *18S rRNA*).

Nitrite assay

Aliquots (50 μl) of culture supernatants were collected and incubated (in triplicate) with equal volumes of Griess reagent (1% sulphanilamide, 0.1% naphthylethylene-diamine dihydrochloride, 2.5% H_3PO_4) at room temperature for 10 min. The plate was read at a wavelength of 540 nm with a microplate reader. Nitrite (NO_2^-) concentration was determined by using sodium nitrite as a standard.

Western blotting

Subjected protein using SDS-PAGE transferred to polyvinylidene difluoride membranes. The membrane was incubated with 2% skim milk for 1 h at room temperature. The membrane was then incubated with primary antibodies overnight at 4°C. Subsequently, the membrane

was incubated with secondary antibodies with horseradish peroxidase for 1 h at room temperature. The specific protein bands on the membrane were visualized.

Statistical analysis
Statistical comparisons among the groups were assessed by one-way analysis of variance (ANOVA). When F ratios were significant ($p < 0.05$), Scheffe's post hoc tests between two groups were done, and $p < 0.05$ were considered statistically significant.

Results and discussion
We first confirmed that quercetin induced cytoprotective effects in RAW264.7 cells. The induction of IL-6 mRNA expression and NO production by LPS/IFN-γ was inhibited by quercetin. Quercetin increased the levels of HO-1 expression at both mRNA and protein levels. Moreover, deficiency of HO-1 cancelled the suppression of IL-6 induced by quercetin, suggesting that Nrf2-HO-1 pathway would be important to exhibit the cytoprotective effects of quercetin. However, the inhibitory effects of quercetin were not completely recovered in HO-1 KO cells. These observations suggest a possibility that other mechanisms might exist besides the enhanced expression of HO-1 by quercetin.

To investigate the effects of quercetin on the expression of chemokines, we examined whether quercetin regulated the expression of CXCL10 (interferon gamma-induced protein 10, IP-10), CCL17 (thymus and activation-regulated chemokine/chemokine ligand 17, TARC), and CXCL2 involved in type 1, type 2, and type 3 immune responses, respectively. While no significant changes in the mRNA expression of CXCL10 and CCL17 were observed, quercetin induced CXCL2 expression at dose-dependent manner. Our results suggest that quercetin may act preferentially on a type 3 immune response. We are now trying to examine time-dependent changes in CXCL2 expression induced by quercetin. We are also investigating the expression of other chemokines.

It is interesting to note that quercetin, which has anti-inflammatory effects, induces CXCL2, an inflammatory chemokine. One hypothesis is that quercetin may help prepare the body for bacterial infection by inducing the expression of CXCL2. Besides Nrf2-HO-1-mediated cytoprotection, this may be a novel prophylactic mechanism of quercetin against pathogens which induced a type 3 inflammation.

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Identification of Regulatory Mechanisms of Colonic pH in Enterotoxigenic Bacteroides fragilis Toxin Secretion

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Introduction

Enterotoxigenic *Bacteroides fragilis* (ETBF) is a pathogenic bacterium that triggers colitis and colorectal cancer in humans. The only known virulence factor of ETBF is B. fragilis toxin (BFT). BFT is an enterotoxin that induces E-cadherin cleavage and subsequent shedding of intestinal epithelial cell layer leading to diarrhea disease.

However, the environmental stimulus for BFT expression is not still elucidated [1]. Furthermore, ETBF-associated inflammation does not occur in small intestine although ETBF is colonized in both small and large intestines. We found that the pH of the small intestine is higher than the pH of the large intestinal. Moreover, the most well-known biological activity of BFT, E-cadherin cleavage did not occur in epithelial cells treated with supernatant cultured with ETBF in alkalic environment. If BFT expression mechanisms regulated by pH were elucidated, this study would help to develop the therapy or drug that cures enterotoxin-induced colitis without side effect.

Materials and methods
Bacterial strains and collection of bacterial supernatants

The three strains of *B. fragilis*, wild-type ETBF (WT-ETBF) expressing BFT, non-toxigenic wild-type *B. fragilis* overexpressing a biologically active BFT (rETBF) and inactive mutated BFT (rNTBF) were used. Three strains were cultured in BHI broth at 37°C under anaerobic condition for another two days. The bacterial supernatants were centrifuged and filtered.

Animal experiment and histology

The C57BL/6 mice were used in this study. The mice were given water containing clindamycin and gentamicin for 5 days, inoculated with *B. fragilis*, and sacrificed after another 7 days. The gastrointestinal tract was harvested and measured by micro pH meter. The intestinal inflammation was examined by H&E-stained sections per mouse.

Cell Culture

The HT29/c1, human colonic epithelial cells were cultured in DMEM supplemented with 10% FBS, 20 mM HEPES and penicillin/streptomycin.

Western blot analysis

Western blot was performed using primary antibody specific to E-cadherin. GAPDH was used as an internal control.

Statistical Analysis

Data in the bar graphs are presented as mean±SEM. All data were analyzed by unpaired t-test (*$P < 0.05$, **$P < 0.01$ and ***$P < 0.001$).

Results
ETBF induces acute inflammation in cecum and large intestine, but not in small intestine

To investigate where ETBF induces inflammation in the intestine, ETBF was orally administrated and whole intestines were extracted. It was elicited that ETBF colonized the small intestine, cecum, and large intestine, but inflammation was observed in cecum and large intestine, not in small intestine (figure 1).
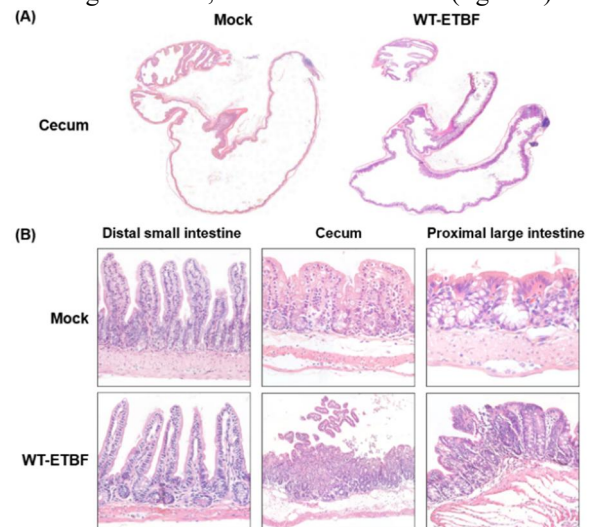

Fig. 1: (A) Images of whole cecum including distal ileum and proximal colon (magnification X0.5). (B) No inflammation was detected in small intestine (magnification X10).

Small intestine has a higher pH than large intestine

We hypothesized that ETBF-induced colitis is determined by the intestinal pH. Initially, the gastrointestinal tracts were extracted and pH was measured. The results demonstrated that the pH of the small intestine shifted increasingly alkaline as it progressed proximally, while the pH of the large

intestine shifted more acidic (data not shown). Furthermore, we infected mice with wild-type ETBF, recombinant ETBF or recombinant NTBF and the pH was measured. Respectively, the trend of alkalinity in the small intestine and acidity in the colon was identical with previous pH measurement (figure 2). In addition, there was no significant difference in the CFU of B. fragilis colonized in small and large intestine.
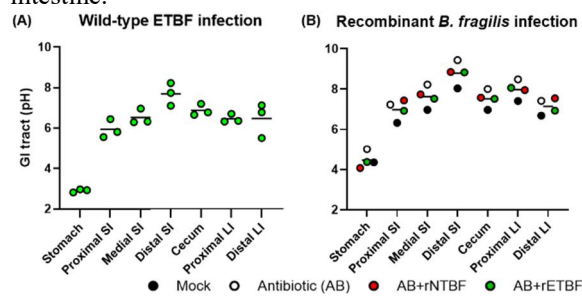

Fig. 2: (A) Intestinal pH in seven parts was measured after WT-ETBF infection for 7 days. (B) Intestinal pH of rNTBF or rETBF-infected mice.

ETBF does not express toxin in alkalic environment

To investigate whether BFT is secreted in an alkaline environment, we cultured ETBF in BHI broth medium adjusted to and alkaline pH. Subsequently, HT29/c1 cells were treated with cultured supernatant. It was observed that the cultured supernatant from ETBF under alkaline broth did not demonstrate E-cadherin cleavage (figure 3).
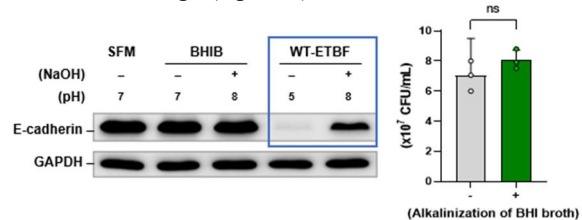

Fig. 3: Western blot analysis of HT29/c1 cells treated with cultured supernatant from normally cultured or pH-adjusted WT-ETBF. There was no significant difference in the number of CFU (ns, non-significant).

The previously secreted BFT is not influenced by pH

To exclude the possibility that secreted BFT is denatured by the alkaline pH of BHIB, the supernatant from normally cultured ETBF was harvested and the pH was adjusted to 5, 6, 7 and 8, respectively. As a result, it was determined by Western blot that the biological activity of BFT exhibits in both acidic and alkaline environments.
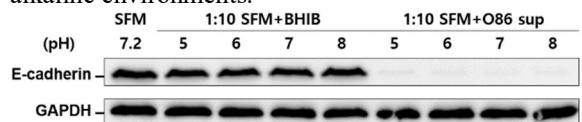

Fig. 4: Western blot analysis of HT29/c1 cells treated with normal or pH-adjusted BFT solution.

ETBF restores BFT secretion when alkalization is stopped

To investigate whether BFT secretion ability is completely lost after pH adjustment, ETBF was acidified pH to 5, 6, 7 and 8 after 24 hours of pH adjustment. HT29/c1 cells were treated with the cultured supernatants and E-cadherin cleavage was detected. ETBF restored BFT secretion ability.
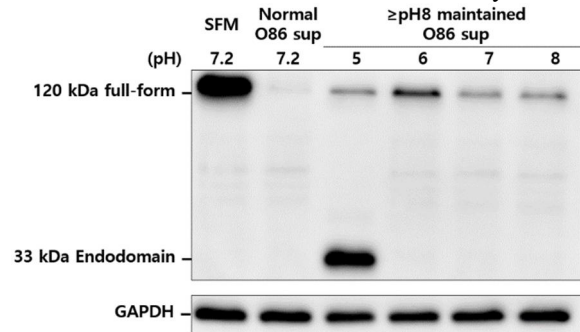

Fig. 5: Western blot analysis of HT29/c1 cells treated with cultured supernatant from ETBF with pH restoration.

B. fragilis alters micro-environment acidic

To examine the pH of micro-environment, BHIB was inoculated with rNTBF or rETBF, incubated for 48 hours and the pH was measured. It is determined that both strains acidified the pH of BHIB extensively in exponential stage.
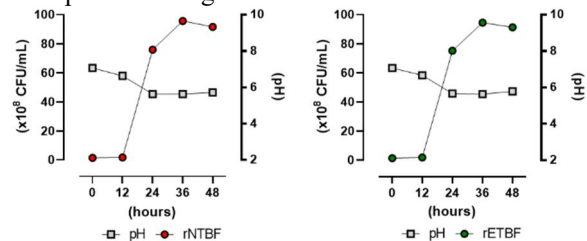
Fig. 6: Measured pH of rNTBF or rETBF-cultured BHIB at indicated time points (6, 12, 24, 36 and 48 hours).

Discussions

According to reported data thus far, regulatory mechanisms by pH were restricted with several bacteria or fungi. The current study identified ETBF, the most responsible pathogen for colitis among microbiome, can be regulated its enterotoxin secretion by environmental pH. These results will help not only to understand the mechanistic pathway of bacterial toxin secretion, but also to develop the cure with pH adjustment without any side effects.

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Analysis of immune responses in NC/Nga mice focusing on lymphocytes

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Introduction

NC/Nga mice, an atopic dermatitis (AD) model, spontaneously develop AD-like skin lesions when raised under conventional environment. NC/Nga mice exhibit type 2-prone immune response characterized by hyperproduction of IgE in association with the development of AD [1]. The B cells of NC/Nga mice also have increased sensitivity to CD40 ligand and IL-4 stimulation, suggesting some modification factors to enhance a type 2 immunity. However, the mechanisms how NC/Nga mice induce type 2-prone immune response is poorly understood. In this study, we investigated the differentiation and proliferation of lymphocytes to explore the basal immune status of NC/Nga mice.
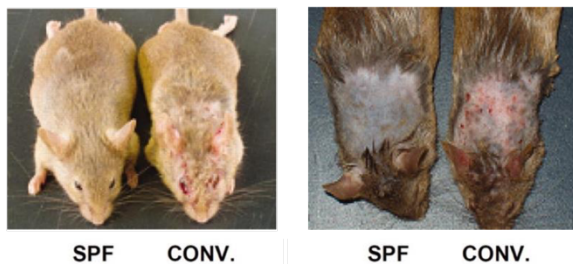

Fig. 1. NC/Nga mice kept in specific-pathogen-free (SPF) surroundings or conventional (CONV.) surroundings (J Immunol 2007;178:584-591).

Method

Mice

Six- to eight-week-old male NC/Nga and C57BL/6 mice were used. Animal experiments were approved by the Animal Experiment Committee of Nagoya University Graduate School of Medicine. All procedures were performed in accordance with the Guidelines for Animal Experimental Experimentation of Nagoya University.

Flow cytometric analysis of lymphocyte differentiation

Bone marrow cells and splenocytes were collected from NC/Nga and C57BL/6 mice. Cells were washed and incubated with anti-CD16/32 antibodies at 4 ℃ for 15 min to avoid unspecific binding to Fc receptors. Cells were then stained with fluorescent-labeled antibodies at 4 ℃ for 20 min. The expression of cell-surface molecules was analyzed by FACSCanto II flow cytometer (BD Biosciences). The data was analyzed and quantified analyzed using FlowJo software program.

Flow cytometric analysis of lymphocyte proliferation

Splenocytes collected from NC/Nga and C57BL/6 mice were labeled with 5 µM 5-carboxyfluorescein diacetate succinimidyl ester (CFSE) (Life Technologies Carlsbad, CA, USA). CFSE-labeled splenocytes were plated at 5×10^5 cells in a 24-well plate and stimulated with 1.0 µg/ml lipopolysaccharide (LPS), 0.5 µg/ml concanavalin A (Con A), or anti-CD3ε/CD28 antibodies for 2-3 days. Cells were then collected, incubated with Fc blocking antibody against CD16/32, and stained with fluorescent-labeled antibodies at 4 ℃ for 20 min. The CFSE signal of gated B cells, CD4+ T cells, or CD8+ T cells was analyzed by flow cytometry on FACSCanto II flow cytometer. The data was analyzed and quantified using FlowJo software program.

Enzyme-linked immunosorbent assay (ELISA)

Splenocytes from NC/Nga and C57BL/6 mice were stimulated with anti-CD3ε/CD28 antibodies for 2-3 days. Supernatant was collected, and production of IL-2 was assayed using a Mouse IL-2 ELISA Ready-SET-Go! Kit (eBioscience, San Diego, CA, USA) according to the manufacturer's recommendations.

Statistical analysis

Statistical comparisons among the groups were performed using one-way analysis of variance (ANOVA). When F ratios were significant ($p < 0.05$), Scheffe's post hoc tests were performed between the two groups, and values of $p < 0.05$ were considered statistically significant. Statistical analyses were performed using StatView software (SAS Institute Inc., Cary, NC, USA).

Results and discussion

First, we examined the proportion of B cells and T cells in splenic lymphocytes, and the number of each lymphocyte subpopulation per spleen. Both the proportion and number of T cells were decreased in NC/Nga mice, while there was little difference in the number of B cells between NC/Nga and C57BL/6 mice. These results suggested that the increased proportion of B cells in NC/Nga mice may be due to the lower number of T cells. Moreover, there is a

possibility that the proliferation and maturation of T cells in the spleen might be impaired in NC/Nga mice. The proportion of CD4$^+$ T cells was increased and that of CD8$^+$ T cells was decreased in NC/Nga mice, suggesting that a dominant CD4$^+$ T cell population may lead to a type 2-prone immune responses in NC/Nga mice.

We next examined the proportion and number of B cells at each stage of differentiation in the bone marrow and spleen. The proportion of mature B cells in bone marrow was significantly increased in NC/Nga mice, while the proportion of pre B cells was slightly decreased. In the spleen, NC/Nga mice showed a marked decrease in the proportion and number of transitional type 1 (T1) B cells and T2 B cells, and a marked increase in the proportion and number of marginal zone B (MZB) cells. These results suggested that B cells in NC/Nga mice might rapidly differentiate into mature B cells due to their modification of rate-limiting step. Furthermore, T2 B cells might differentiate more dominantly into MZB cells in NC/Nga mice.

Next, we investigated the proliferation of splenic lymphocytes in response to LPS, Con A, or anti-CD3ε/CD28 antibodies. Higher B-cell and T-cell proliferations in response to LPS or Con A were observed in NC/Nga mice, respectively. Moreover, NC/Nga mice exhibited higher T-cell proliferation and IL-2 production stimulated by anti-CD3ε/CD28 antibodies. These suggested that increased production of IL-2 might enhance cell proliferation in NC/Nga mice compared to C57BL/6 mice.

In conclusion, our results suggest the possibility that a unique differentiation pattern and accelerated proliferation of lymphocytes might cause potent type 2-prone immune response in NC/Nga mice.

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Department sessions

Physical Therapy				
	Opening remarks	Prof. Hideshi Sugiura	Nagoya	
Session I				
13：30-14：30	Chair	Prof. Yasushi Uchiyama	Nagoya	
		Masahiro Nishimura	Nagoya	COP COM Coordination Is Related to a Process of Acceleration Drive on Gait Initiation in Community Dwelling Elderly People
		Akira Omi	Nagoya	Effects of auditory stimulation on gait orientation
		Yumika Suzuki	Nagoya	Analysis of the molecular mechanisms underlying the cell surface localization of M-cadherin during skeletal muscle regeneration
	Intermission (20 min)			
Session II				
14:45-15:50	Chair	Prof. Sanghyun Cho	Yonsei	
		Lingchao Xie	Yonsei	Ankle Strategies for Step Aside Movement during Straight Walking
		Wonjun Oh	Yonsei	Who are the Best Candidates for Robotic Gait Training Rehabilitation in Hemiparetic Stroke?
		Yunhwan Kim	Yonsei	Long term Effects of Deep Learning Digital Therapeutics on Sustainable Pain and Movement in Low Back Pain Management
	Closing remarks	Prof. Sanghyun Cho	Yonsei	
	Awarding of certificates	Prof. Hideshi Sugiura	Nagoya	

COP-COM Coordination Is Related to a Process of Acceleration Drive on Gait Initiation in Community Dwelling Elderly People

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[Introduction]

Gait initiation is a complex motor task that gene-rates transitioning from a static standing position to a dynamic state characterized by gait cycle. This process demands a higher degree of control and complexity compared to steady-state gait (SSG) and presents potential fall risks associated with postural control during gait initiation [1,2]. To address this critical issue, numerous studies have been conducted, focusing on the stability of gait initiation from the perspective of postural control.

One fundamental aspect of postural control during gait initiation is the control of the center of mass (COM) within a base of support (BOS), which is the area of contact with the supporting surface. This control is essential to maintain stability throughout the transition from standing to walking. Additionally, the center of foot pressure (COP) plays a pivotal role in controlling the floor reaction force, ensuring that the COM remains within the boundaries of the BOS [3]. An important concept used to assess postural control ability is COP-COM coordination which provides insights into the coordination between COP and COM during this critical phase of movement. The process requires when the trajectory of COM alternately passes between COP, which is controlled by each supporting leg. This concept is crucial in understanding the mechanisms behind successful gait initiation [4].

In recent years, there has been a lot of research on the use of wearable devices to acquire biometric information and take up gait analysis, with small accelerometers in particular being a representative tool. The information obtained from acceleration data is trunk sway, and trunk acceleration measured with an accelerometer attached to the lumbar spine (L3-4) as an indicator of gait stability has established reliability and validity [5]. Therefore, it is expected to be a tool for sensitivity and convenience in gait analysis. In addition, the information represented by trunk acceleration includes a gait strategy and propulsive process of the stance phase [6,7] in the anterior-posterior direction, the forefoot rocker timing and propulsive preparation [8] in the vertical direction, and the symmetry of the entire gait cycle and trunk stability [8] in the lateral direction, thus visualizing various postural adjustment processes from the three axes.

Building upon this foundation of knowledge, the aim of the present study is to investigate the involvement of COP-COM coordination in the process of acceleration control during gait initiation among community-dwelling elderly people.

[Methods]

11 young people (22.2±1.4 years) and 23 community-dwelling elderly people (71.9±4.3 years) walked 5 times of 12m gait as self-selected speed. COM were detected from 15 markers on subject's body by using motion capture system. COP was traced by 2.4m foot pressure distribution sensor. "COP-COM separation" was calculated as root mean square of a period from starting motion to 3rd step in the anteroposterior (AP) and mediolateral (ML) direction. Acceleration in tri axis was measured by a gyro combined accelerometer (MVP-RF8, MicroStone), which placed at the torso (height of L3 spinous process [5]. Both acceleration and angular velocity components were used to detect trunk acceleration, with correction for gravitational acceleration based on the Euler angle principle. The measured data were processed with Butterworth low-pass filter (4th order, cutoff frequency 12.5Hz [9]). After post process, acceleration data was calculated as root mean square of a period from starting motion to 3rd step (RMS ML, RMS V RMS AP, respectively). To compare sensitive difference of balance ability, we divided elderly people into two groups; elder(H) and elder(L), based on Timed Up and Go Test (TUG) time (Table1). We compared each outcome with applying one-way ANOVA and Bonferroni Method as post-hoc test. Multiple regression analysis was executed for elderly group as explanatory variables were

"COP-COM separation" in each direction and age and response variable was acceleration RMS in each direction. Significant level was set as p<0.05 (included adjustment).

Table1 Subjects' characteristics

	Young (n = 11)	Elder(H) (n = 12)	Elder(L) (n =11)	P-value(All)
Age(year)	22.2±1.4	70.9±3.9	73.0±4.6	<0.01
Height(cm)	167.8±8.6	163.1±6.9	162.3±7.2	n.s
Weight(kg)	57.3±10.2	61.3±9.2	60.2±14.4	n.s
TUG COM(s)	—	8.14±0.48	9.97±0.70	<0.01
Mean±SD				

* < 0.05 ** < 0.01 *** <0.001

[Results]

"COP-COM separation" in the AP direction of elder group with low performance of TUG was significantly lower than the others(p<0.001, Fig.1). RMS V, young group was significantly larger than the other two groups (p<0.05, p<0.001, respectively Table2); RMS AP, young, elder (H), and elder (L) groups were significantly larger, in that order (p<0.01, p<0.05, .respectively Table2).
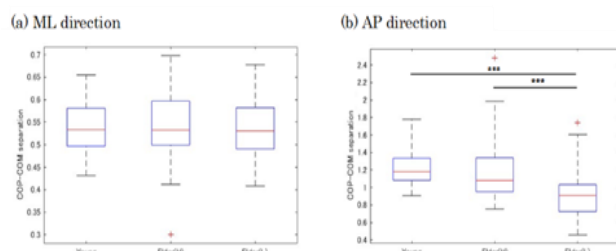

Fig.1 COP-COM separation in each direction is described as above. In ML direction, there are no significant difference among 3 groups. In AP direction, Elder(L) is significantly lower value than other 2 groups (p<0.001).

Table2 Acceleration RMS in 3-axis direction

	Young (n = 49)	Elder(H) (n = 52)	Elder(L) (n = 49)	P-value
RMS ML(m/s^2)	1.07±0.13	1.02±0.19	1.03±0.28	n.s
RMS V(m/s^2)	1.86±0.17	1.67±0.38	1.55±0.40	<0.001
RMS AP(m/s^2)	1.59±0.38	1.40±0.19	1.27±0.21	<0.001

[Discussion]

In terms of COP-COM coordination, a previous research for healthy elderly people who were tasked to cross over an obstacle reported as a similar result as our results [4]. Besides, young people had greater value than elderly people in the AP direction and elderly people with high risk of fall were lower than those with low one in the ML direction when they did continuous voluntary movement in standing [10]. Interestingly, "COP-COM separation" in the ML direction for subjects who are lower fall risk is estimated to be around 60% [4]. We suspect that the

difference was not seen in the ML direction, where the risk of falling is more easily detected for patients or those who have a severe balance disfunction, but only in the AP direction.

Lower COP-COM coordination was found to limit COM acceleration for COM transfer on gait initiation [11]. One factor is likely to be a decrease in functional BOS due to age-related decline in postural control [12]. It may suppose that an interaction between COP and COM on gait initiation could not be successfully activated to the forward shift of COG and was not linked to effective kinematic control during walking. We propose that a main interpretation of this study is elderly people with reduced balance ability adjusted their walking speed related to acceleration drive by compensatory reduction of distance between COP and COM to maintain stability, and may be supported as an indicator to estimate dynamic postural control ability on gait initiation.

In summary, COP-COM coordination of healthy older adults on gait initiation is likely to be sensitive in the AP direction, suggesting that it contributes to acceleration control leading up to SSG. This fact provides a valid quantification of dynamic postural control ability on gait initiation.

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Effects of auditory stimulation on gait orientation

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Introduction

Postural control is based on the use of spatial positional information from visual, vestibular, and proprioceptive systems.[1] The central nervous system (CNS) receives feedback from these sensory systems regarding body orientation and selectively activates muscles.[2] Recently, it has been reported that in addition to these senses, hearing also has an important influence on postural control.[3][4] Hearing helps us to know where we are in our environment and it allows us to track our changing position dynamically over space and time and auditory stimulation can provide the effect similar to the benefits associated with visual fixations or light touch.[4] Some studies show that hearing loss increases anxiety when walking and decreases walking speed and stride length and people with hearing loss have three times the risk of falling compared to those without hearing loss. [5][6]

Some studies show the interaction between standing balance and auditory stimulation and auditory stimulation can be used by human subjects to decrease postural sway.[7][8]

However, the relationship between auditory stimulation and gait orientation has not been clarified

Thus, this study aim is to clarify the effects of auditory stimulation on gait orientation.

Methods

The study group consisted of 19 young, healthy subjects: (11men, 8women, age: 21.7±0.7 years, height: 165.8±7.8cm, weight: 55.0±7.5kg).

Minimum hearing thresholds were measured at four frequency bands of 500 Hz, 1000 Hz, 2000 Hz, and 4000 Hz in both ears using an audiometer MT JIS T1201-1 (As One.)

The main experiment was a 10-meter walk experiment. Subjects were asked to walk in the direction of a sound coming from any of three locations with their eyes covered with an eye mask. The sound locations were left forward, forward, right forward (forward, plug direction, no plug direction). First, subjects walked 3-meters without sound, and, when they reached the 3-meter mark, we started playing sound that is white noise. The experiment was performed three times for each subject in each direction in a random order. We played an intermittent sound of 65dB. We allowed the subjects to walk toward the target sound and then measured differences in distance from the target arrival point, and compared this distance between with earplugs and without ear plugs.
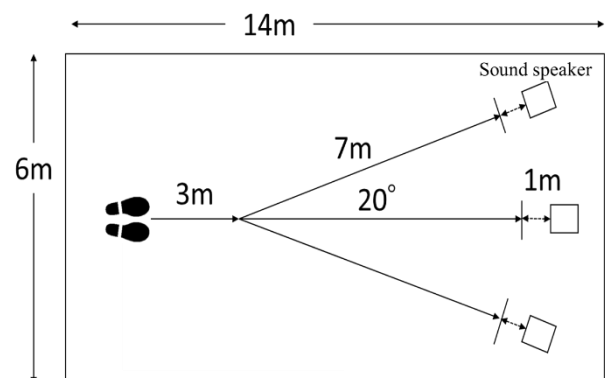

Figure1: experimental environment

Results

Without earplug, the average hearing threshold was 13.3±4.2dB and with earplugs, the average hearing threshold was 34.4±6.1dB (Table1). The difference from the target arrival point was greater with earplugs than without earplugs (Table2).

Table1: hearing thresholds

	without ear plug (n=19)	with earplug (n=19)
hearing thresholds (dB)	13.3±4.2	34.4±6.1

Table2:gap from the target

(cm)	forward	no plug direction	plug direction
without ear plug (n=19)	22.8±20.6	29.3±34.2	28.5±29.2
with earplug (n=19)	42.2±40.9	59.0±60.5	54.0±47.3

Discussion

The difference from the target arrival point was greater with earplugs than without earplugs (p<0.05). Vause reported 25% increase in error in sound localization when using earplugs compared to not using earplugs in a test of sound localization.[9] In addition, Wanrooij showed the error of sound localization was 10° to 20° larger with earplugs than without earplugs.[10] Furthermore, it has also been reported that wearing earplug increase postural sway.[11] These results show that hearing loss decrease sound localization and increase gap from the target

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Analysis of the molecular mechanisms underlying the cell surface localization of M-cadherin during skeletal muscle regeneration

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Introduction

Skeletal muscle has various physiological functions in vivo. It has also self-regeneration ability from injury, which is often the subject of physical therapy. Thus, in my view, understanding the molecular mechanisms of musculoskeletal regeneration leads to a better comprehension of muscular disorders.

The process of the muscle regeneration from damage is composed of multiple steps. When skeletal muscle is injured, first, muscular stem cells, 'satellite cells', localizing around the damaged muscle fibers are activated to become myoblasts to start cell growth. Second, myoblasts migrate into the damaged area and fuse to each other to form multi-nucleated myotubes that are precursors for myofibers. By repeating these processes, huge, functionally intact myofibers are regenerated. (fig.1) [1].
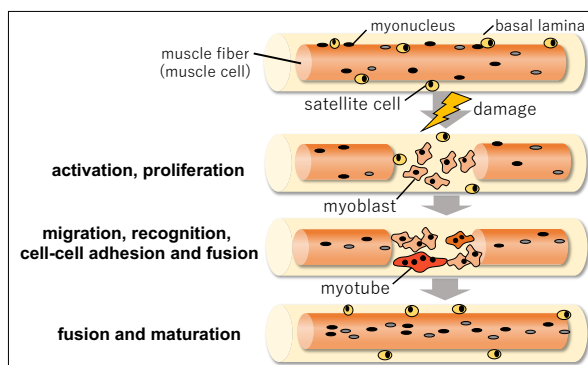

Fig.1 The process of muscle regeneration

In the complex regeneration processes, it is thought to be necessary for myoblasts to recognize and adhere to the similar type of cells as fusion partners. The cell-recognition and adhesion process should be strictly regulated, and I thought that promotion of this step by medical interventions could improve the rate of myoblast fusion and further skeletal muscle repair.

M-cadherin (Mcad) is one of the adhesion molecules expressing specifically in muscle cells and its expression level is transiently up-regulated during muscle regeneration [2]. Because cell surface localization of Mcad should be required for its recognition of neighboring cells and its function as an intercellular tethering machinery, intracellular localization could be controlled under induction of myogenesis. Few studies, however, have quantified the functional Mcad on the plasma membrane, and the mechanisms of intracellular transport and plasma membrane localization of endogenous Mcad remain unclear.

In order to investigate the regulatory mechanisms of Mcad intracellular transport, I tried to develop a new tool to quantify the amount of Mcad localized on the cell surface of myoblast using Nano-Glo® HiBiT system (Promega Corporation) (fig.2).
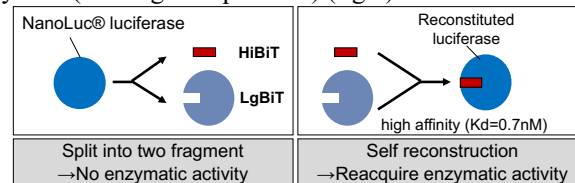

Fig.2 Nano-Glo® HiBiT system

First, I inserted the HiBiT tag of 11 amino acid residues into the extracellular domain of Mcad to construct an 'Mcad-HiBiT' artificial gene, and Mcad-HiBiT was transfected into C2C12 cultured myoblast cells. Then, LgBiT protein was added to the C2C12 cells expressing Mcad-HiBiT gene. LgBiT bound to the HiBiT region of cell-surface Mcad-HiBiT became active luciferase enzyme and was detected by measuring its activity. The luminescence intensity reflects the number of Mcad localized on the cell surface (fig.3).

Using the newly established tool to monitor the amount of cell-surface Mcad, chemical compounds library was screened to search for compounds that could affect the Mcad surface expression.
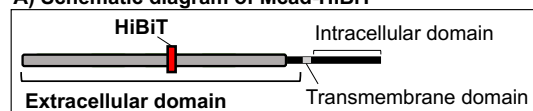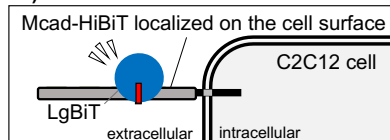
Fig.3 Concept of the new tool established in this study.

Methods

Cell culture: C2C12 cells were cultured in the growth medium (GM) containing DMEM (Wako) with 12% Fetal Bovine Serum (FBS, biowest), 1% penicillin-Streptomycin (Wako) at 37°C under 5% CO_2. Muscle differentiation of C2C12 cells were induced by replacing the medium with differentiation medium (DM): DMEM supplemented with 2% horse-serum (Sigma-Aldrich) and 1% penicillin-streptomycin.

Chemical compound screening: Drug screening was performed using SCAD inhibitor kits (kit I, ver.4; kit II, ver. 2.1; kit III, ver.1.7; kit IV, ver2.4) obtained from the Molecular Profiling Committee, Grant-in-Aid for Scientific Research on Innovative Areas "Platform of Advanced Animal Model Support (AdAMS)" from the Ministry of Education, Culture, Sports, Science and Technology, Japan (JSPS KAKENHI Grant Number JP 16H06276).

C2C12 cells stably expressing Mcad-HiBiT gene were plated at 2×10^4 cells/well in a 96well plate with white opaque walls and transparent bottoms (PerkinElmer). After incubation in GM for 24 h, myogenic differentiation was initiated by switching the medium to DM for more 24 h. Then a total of 364 drugs were added to each well at a final concentration of 2 μM. The compounds were dissolved in DMSO at a final concentration 0.1% and same amount of DMSO was added to the control well. After 24 h incubation, cells were fixed in 4% paraformaldehyde, washed with PBS, and 2μg LgBiT were added each well. After incubation excessive amount of LgBiT was washed out and the amount of the LgBiT-Mcad-HiBiT complex localized at the cell surface was detected using the Nano-Glo® Luciferase assay system (Promega Corporation), following the manufacturer's instructions. The luminescence intensity was measured using a luminometer ARVO MX1420 (PerkinElmer). After the luminescence measurements, nuclei were stained with Hoechst33342 to count the cell number automatically using BZ-X800 (KEYENCE).

Results

To explore chemical compounds that affect the intracellular localization of Mcad, the 364 inhibitors to various kinds of cellular enzymes were screened. Relative luminescence intensity divided by the number of the cells was shown with a negetive control (DMSO) (fig.4). Any chemical compounds that vary the cell number by more than 20% compared to control, were excluded. The result showed 9 compounds greately affect the amount of Mcad localized on the cell surface (Table.1).
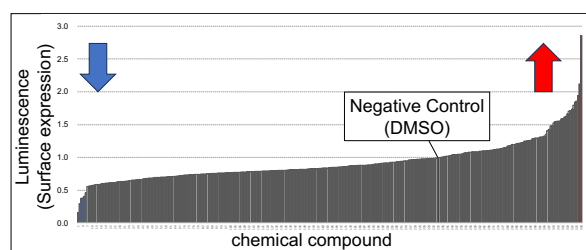

Fig.4 The amount of the Mcad localized on the cell surface.

Table.1 The list of chemical compounds with large variation

Luminescence	inhibitor	Target enzyme/cellular effect
0.156	Thapsigargin	Ca^{2+}ATPase
0.297	anisomycin	p38 MAPK activator
0.376	brefeldin A	golgi inhibitor
0.384	Nigericin	K^+ ionophore
0.410	Bafilomycin A1	V-ATPase
0.459	Cdk2/9 inhibitor	CDK2/9
1.000	DMSO	(negative control)
1.939	Y27632	ROCK
2.122	Scriptaid	HDAC
2.855	MG-132	proteasome

Discussion

In this study, new assay tool that can selectively detect Mcad localized on the cell surface was established. And some chemical compounds were found to affect the intracellular localization of Mcad during muscle regeneration.

Scriptaid, an inhibitor of HDAC (histone deacetylase), was reported to decrease dexamethasone-induced muscle atrophy, and HDAC itself involves induction of muscle atrophy due to muscle disuse [3,4]. So, it is interesting if HDAC is also involved in the function of Mcad during muscle regeneration in vivo.

In the future, further screening of molecules and genes using the newly established screening tool will provide us important information concerning the molecular regulatory mechanisms on the myogenic differentiation. Moreover, accumulation of such knowledge is supposed to contribute the development of effective clinical interventions for patients who need physical therapy.

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Ankle Strategies for Step-Aside Movement during Straight Walking

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Introduction

Step-aside movement (dodging step) during walking is a common maneuver to avoid obstacles; however, it is associated with fall risk owing to differences in neural control mechanisms and ankle strategies compared to straight walking. In our previous study, the mechanisms of ankle muscle contraction, foot center of pressure (CoP) displacement, and ground reaction force (GRF) generation in step-aside movements during standing were explored, excluding the influence of walking [1]. The current study aimed to extend previous findings by studying these mechanisms during straight walking, offering potential avenues for understanding obstacle avoidance.

Methods

Twenty healthy young male participants were recruited, experimental trials were conducted in a 36 m straight corridor, and the participants walked in two conditions at normal walking speed (1.15 ± 0.13 m/s) between three parallel lines of yellow pinstripe tape on the corridor floor at shoulder-width distances as per walking guidelines [16,17]. The participants walked straight between the left and middle guidelines; ten steps were statistically analyzed.

Afterward, the participants walked straight within the left and middle guidelines again, but this time, they were instructed to step aside to the right to walk between the middle and right pinstripe tapes at a self-selected time. Since a change in direction must be planned in the previous step [18], participants dictated verbal cues of "1, 2, 3" to themselves while they made step-aside movements. The specific foot placement of the step-aside movement and timing of the self-verbal cues are shown in Figure 1.

Figure 1. The sequence of "step-aside to the right" during straight walking. The numbers indicate the self-verbal cue.

The participants performed three sessions for both walking conditions, and only ten step-aside movements in the third session were recorded and analyzed. The data from the first and last steps of each condition were not included in the statistical analysis.

The present study tested the differences between the conditions in EMG muscle activity, CoP displacement, and GRF by statistically examining the entire time series using one-dimensional statistical parametric mapping (SPM1d) in Python 3.8 (www.python.org), using the open-source software package SPM1d 0.4.8)

Result

The two-tailed paired t-test revealed significant increases in EMG activation of all three ankle muscles during the left push and right loading phases of the step-aside movement compared to straight walking.

Figure 2. (a,c,e) Grand mean patterns for normalized TA, PL, and SOL EMG amplitudes of the step-aside to right movement (red) and the straight walking (black) in the left push phase. The grey bars indicate the region of interest (ROI). (b,d,f) SPM{t} results depict the differences in muscle activities between the two conditions. The critical threshold t* (wide dashes) exceeded during (b) 37.2–51.4%, 56.2–59.9%, and 61.7–63.8%, (d) 34.7–51.8%, and 58.2–59.9%, (f) 38.9–50.0% of the gait cycle. p values < 0.05 (*), <0.01 (**), and <0.001 (***) indicate significant differences between step-aside movement (SA) and straight walking (SW).

In the left push phase, the two-tailed paired t-test indicated a significant decrease in foot CoPx displacement at 19.0–26.5%, and a significant increase at 37.0–58.9% of the gait cycle (Figure 5b). Furthermore, foot CoPy displacement significantly increased from 19.0–28.9% and 36.3–53.9%, with a

significant decrease at 60.3–61.8% of the gait cycle. However, the right-foot CoPx displacement significantly decreased only during 7–22.0% of the gait cycle compared to straight walking (Figure 5f).
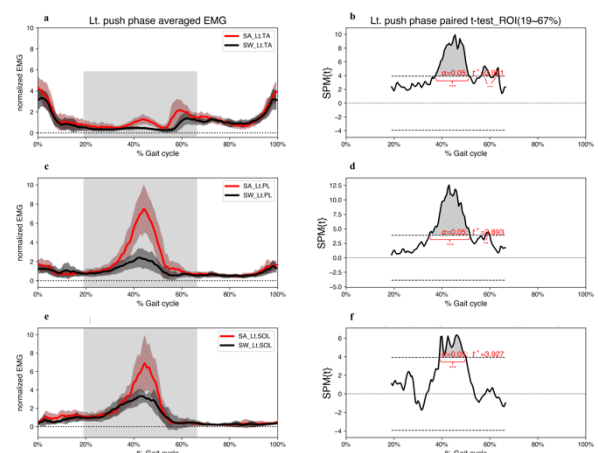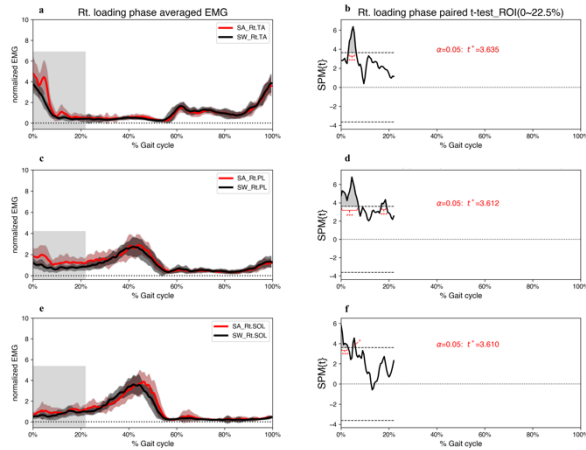

Figure 3. (a,c,e) Grand mean patterns for normalized TA, PL, and SOL EMG amplitudes of the step-aside to right movement (red) and straight walking (black) in the right loading phase.

The SPM{t} trajectory of the left-foot forefoot GRF (F-GRF) and heel GRF (H-GRF) crossed the critical threshold downward, representing a significant decrease compared to straight walking (Figure 4b,d). Additionally, the SPM analysis revealed that during the right loading phase of the step-aside movement, a major region of the SPM{t} trajectory of the right-foot
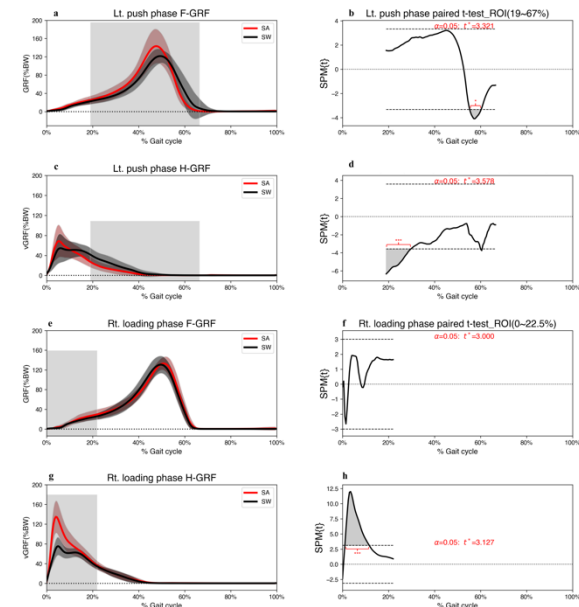

Figure 4. (a,c,e,g) Grand mean patterns for CoP displacement of the step-aside to the right movement (red) and the straight walking (black) in the left push and right loading phase.
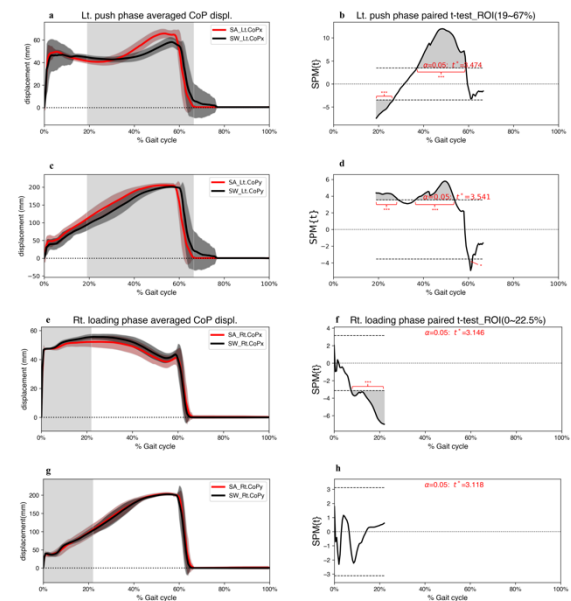
Figure 5. (a,c,e,g) Grand mean patterns for F-GRF and H-GRF of the step-aside to the right movement (red) and straight walking (black) in the left push and right loading phase.

H-GRF exceeded the critical threshold, signalling a remarkable and significant increase in step-aside movement (Figure 4h).

Discussions

The study's findings indicate that during step-aside movements, there is significantly higher bilateral ankle muscle activation, particularly in the left PL muscle during the left push phase. This contrasts with straight walking. The analysis also supports the hypothesis that the CoP trajectories significantly differ during the left push phase. These differences are observed in both CoPx and CoPy trajectories.

During the right loading phase of step-aside movements, the muscle activation patterns supported the hypothesis of increased ankle stability during initial foot contact. Additionally showed decreased CoPx displacement but minimally changed in CoPy displacement.

During the pre-swing period of step-aside movements, greater muscle contractions are observed in the TA and PL muscles compared to straight walking, contributing to toe clearance. Participants shift their body weight earlier to the left during step-aside movements, similar to anticipatory postural adjustments (APA), which generate forward propulsive force. This shift involves moving the left-foot CoP in the opposite direction, benefiting PL muscle contractions for right-side propulsive force.

Additionally, the left-foot CoP moves further and ends the displacement sooner than in straight walking, facilitating longer strides.

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Who are the Best Candidates for Robotic Gait Training Rehabilitation in Hemiparetic Stroke?

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Introduction

RAGT (Robot-Assisted Gait Training) has gained popularity for improving gait function in hemiparetic stroke patients, but the ideal timing and patient characteristics for its effectiveness remain unclear [1]. There's a need to determine the best initial ambulation level (FAC) for RAGT in stroke patients [2]. Some suggest that exoskeletal RAGT, like Lokomat and Walkbot, may be more effective for patients with FAC < 2 (weight supporting group), while overground walking training is recommended for FAC ≥ 2 (non-weight supporting group) [3]. Studies on Lokomat and Walkbot RAGT have shown varying results in stroke patients [4-10]. To address this variability and accommodate patients with FAC levels ranging from 0 to 4, we developed a Walkbot RAGT offering interactive guidance and progressive resistance modes, along with real-time feedback on joint kinetics and kinematics [4]. This study aims to evaluate the effects of Walkbot RAGT on sensorimotor recovery in subacute stroke patients with FAC <2 (low initial functional ambulation category [LFAC]) and FAC ≥ 2 (high initial functional ambulation category [HFAC]) using FMA, MAS, BBS, TIS scores, as well as the number of steps and walking distance. We hypothesize that RAGT will lead to similar improvements in both groups.

Method

We included 57 subacute stroke patients who participated in RAGT at Cheong Dam Hospital, Seoul, South Korea, between June 2017 and September 2019. Inclusion criteria covered age, stroke type, and physical parameters, while exclusion criteria involved various medical and physical conditions.

- Clinical Outcome Measures
1. FAC: A 6-point scale assessing ambulation ability.
2. FMA Scale: Evaluating sensorimotor impairment in hemiparetic stroke patients.
3. MAS: Assessing spasticity in various neurological conditions.
4. BBS: Evaluates balance during specific tasks.
5. TIS: Assesses trunk motor impairment after a stroke.
6. Number of Walking Steps and Walking Distance: Measured using the Walkbot system.

- Intervention: Both groups received RAGT three times/week for six weeks using the Walkbot-G system. The system provides real-time feedback and adjusts support as needed. Conventional physical therapy was also administered twice daily.

- Statistical Analysis: Descriptive statistics, power analysis, and ANCOVA were used to analyze the data. The significance level was set at 0.05, and data were adjusted for outliers and missing values.

Results

ANCOVA test found a significant difference in FMA scores between the LFAC and HFAC groups, with higher sensorimotor recovery in the HFAC group. ANCOVA analysis showed no significant difference in MAS scores between groups and time effect. ANCOVA demonstrated that RAGT intervention significantly changed the balance (BBS scores) in both groups, with greater balance improvement in the HFAC group. TIS results indicated that RAGT intervention significantly improved trunk stability (TIS scores) in both groups, with greater improvement in the HFAC group. Number of Steps showed a significant time effect in both groups, but no group differences were observed. Walking Distance also showed a significant time effect in both groups, with no group differences.

Table 1. Clinical outcome data difference between LFAC and HFAC groups.

	LFAC		HFAC		P-Value		
	Pre Test	Post Test	Pre Test	Post Test	Time Effect	Between Groups	Time× Group
FMA	12.73 ± 16.15	15.5 ± 17.15	32.59 ± 24.25	36.37 ± 24.94	0.404	0.000**	0.303
MAS	1.57 ± 0.82	1.47 ± 0.73	1.37 ± 0.74	1.37 ± 0.74	0.805	0.363	0.000
BBS	3.2 ± 3.46	7.23 ± 4.6	15.48 ± 10.33	27.19 ± 6.25	0.000**	0.000**	0.000**
TIS	3.97 ± 5.33	4.87 ± 5.59	9.11 ± 5.41	12.96 ± 5.26	0.026**	0.000**	0.167
STEP	646.4 ± 347.67	1043.83 ± 346	654.15 ± 340.79	1125.07 ± 311.58	0.000**	0.482	0.000
DIS	350.43 ± 185.58	564 ± 183.85	364.74 ± 223.96	590.22 ± 216.55	0.000**	0.593	0.000

Data are presented as the mean ± standard deviation. Abbreviations:; FMA, Fugl–Meyer assessment; MAS, Modified Ashworth scale; BBS, Berg Balance Scale; TIS, Trunk Impairment Scale; STEP, number of steps; DIS, walking distance. ANOVA, analysis of variance ANCOVA, analysis of covariance * P < 0.05. ** P < 0.01.
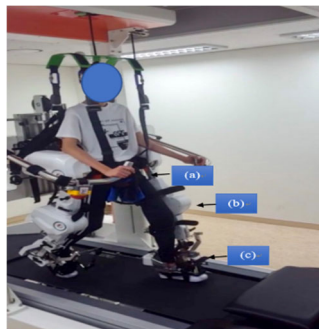

Figure 1. Walkbot exoskeletal system. (a) hip joint actuator including servomotor; (b) knee joint actuator including servomotor; and (c) ankle joint actuator including servomotor.

Discussions

This study investigated the effect of RAGT on sensorimotor recovery function using the FMA scale, spasticity based on the MAS, balance based on the BBS, and trunk stability based on the TIS, as well as number of walking steps and walking distance in subacute stroke patients with low or high initial FAC. As anticipated, regardless of the baseline FAC, both groups demonstrated significant improvements in sensorimotor, spatiotemporal, loss of balance, and trunk stability function following Walkbot RAGT intervention. Most importantly, the current findings dispute the notion that exoskeletal RAGT using Walkbot can provide clinically meaningful changes in balance and gait function in subacute hem-iparetic stroke patients with low or high initial FAC. To our best knowledge, there is no previous study on this in the literature, which makes it difficult to compare our outcome measure data in subacute stroke patients with low or high initial FAC.
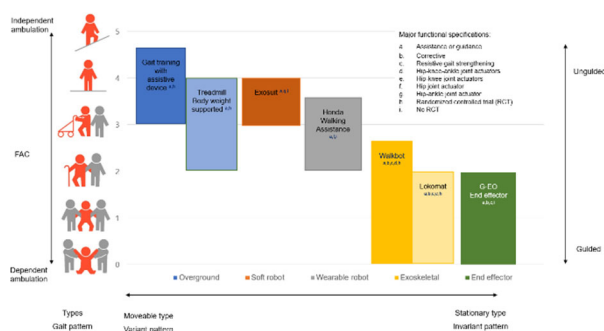

Figure 2. New robotic-assisted gait training schematic guideline based on baseline functional ambulatory category level.

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Long-term Effects of Deep Learning Digital Therapeutics on Sustainable Pain and Movement in Low Back Pain Management

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Introduction

Low back pain (LBP) involves multifactorial sources of pain including faulty posture, and movement, sleep disturbance, and depression and other factors. In particular, essential movement including bending, standing, lifting, twisting (rotation) and walking are commonly impaired during ecological activities of daily living (ADL) and social participation, compromising quality of life in people with LBP. Derangement syndrome may involve mechanical obstruction of the affected joint structure that compresses the intervertebral disc and nerve root, resulting in either centralized or peripheralized pain during repetitive abnormal lumbar movement [1]. To mitigate the spinal movement impairments, a variety of manual therapeutic approaches including massage, electrotherapy, manipulation, mobilization, mechanical traction and therapeutic exercise have been used [2]. However, to fight the prolonged coronavirus disease 2019 (COVID-19) pandemic, a recent healthcare model has adaptively reformed from the conventional contact (hands-on) approach to the untacked approach to prevent the collapse of national health care systems worldwide [3]. Hence, the clear need exists to develop the untacted therapy system for effective and sustainable monitoring, diagnosis, and treatment in people with LBP. The purpose of the present study was to compare the effects of the deep learning-based digital application (Dr.AI) with digital application physical therapy (DPT) on back pain intensity, limited functional disability, radicular symptoms, and quality of life as well as post-questionnaire for satisfaction questionnaire when compared to conventional physical therapy (CPT) in 100 patients with low back pain.

Methods

A convenience sample of 100 participants (mean age 35.5±8.8; 20 females) was recruited and underwent either DPT or CPT for 30-min sessions, 3 times a week over a 4-week period. Outcome measures included the (1) Oswestry disability index (ODI), (2) Quebec Back Pain Disability Scale (QUE), (3) Roland–Morris disability questionnaire (RMDQ), (4) numeric pain rating scale (NPRS), (5) short-form 12 (SF-12), and (6) post-intervention satisfaction questionnaire.

The DPT using Dr. AI provided an individualized intervention video, which followed the exercise as outlined in the mechanical diagnosis and therapy (MDT) exercise theory and dynamic neuromuscular stabilization (DNS) along with a video, such as anterior/posterior derangement syndrome, dysfunction syndrome, postural syndrome, and prone hip extension. Participants observed the centralization vs. peripheralization and better/worse response to the exercise after the exercise. However, if peripheralization or pain worsened, the AI recommended other exercises.

Fig 1. Dr.AI smartphone application

The CPT intervention comprised the therapeutic modalities (heat, ultrasound, and TENS), mobilization, manipulation, and therapeutic exercises (stretching, sling exercise, and core stability training), and was consistently delivered by the two licensed, experienced physical therapists (6-12 years) according to the standardized intervention protocols.

Statistical analysis included analysis of variance (ANOVA) to determine the intervention-related changes in the outcome variables: (1) ODI, (2) QUE, (3) RMDQ, (4) NPRS, (5) FMS (6) SF-12. Independent t-tests were used to compare post-questionnaire results for post-intervention satisfaction between the DPT and CPT groups.

Results

Fig 2. Clinical outcome measurements
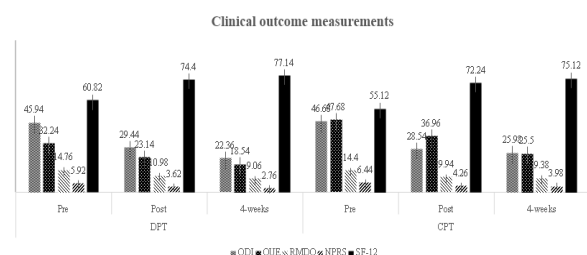
The ANOVA revealed a positive effect on clinical outcome measures following 8 weeks of both DPT and CPT. Especially, the DPT group demonstrated significantly greater enhancements in the post-intervention satisfaction compared to the CPT group (Figure 2 and Table 2).

Table. 2: Post-intervention satisfaction questionnaire.

	DPT	CPT	p-value
Accessibility	4.67±0.48	3.27±0.84	0.02*
Effectiveness	4.09±0.72	4.39±0.75	0.1
Cost	4.91±0.29	2.76±0.97	0.01*
Sustainability	4.06±0.75	3.97±0.88	0.68
Real-time feedback	3.58±0.75	2.42±1.39	0.01*

Discussion

Pain and associated disability analysis showed that enhancement was significantly different in ODI, NPRS, and RMDQ between the DPT and CPT intervention, respectively. It is possible that the pain and associated disability were improved in both groups because CPT (passive manual reduction) and DPT (patient self-reduction) may have improved pain and associated disability in both groups due to maligned soft tissue and lumbar disc prolapse [4].

ADL analysis showed that both DPT and CPT lead to significant improvements in QUE. Mechanism for ADL improvement is that CPT and DPT interventions both provide knowledge of results (KR) and KP feedback, where audiovisual motor learning strategy (motor and clinical) improvements are related to better movement, flexibility, and ADL abilities. Presumably, these ADL processes are more involved in making use of critical information about moving and adapting motor behavior to improve efficiency [5]. The results of this research suggest that providing incremental real-time feedback during progress toward a goal, along with the use of activity monitors, helps patients adjust their behavior in time to make better progress and thus may be more helpful compared to traditional feedback [6].

The QOL analysis demonstrated that both interventions were equally effective in enhancing SF-12. DPT and CPT would increase patient motivation and life-activity in the intervention, making it more effective in the short and medium terms. Providing incremental real-time feedback during progress toward a goal, along with the use of activity monitors, helps patients adjust their behavior in time to make better progress. Use of such activity monitors has been shown to improve level of physical activity, thus enhancing improvement in function and decrease in pain in patients with LBP [7]. Mobile devices are personal and constantly accessible to patients, the use of DPT, specifically smartphone applications, is considered a potentially useful way for patients to monitor their condition, as it enhances patients' ability and their willingness to engage in self-management, thus improving treatment compliance [6, 7].

The post satisfaction questionnaire analysis showed more significant differences in accessibility, cost and real-time feedback in the DPT group compared to the CPT group. The findings of this study seem to be consistent with the opinion that telerehabilitation is a viable link that may help remedy the challenges of barriers of distance, time, and travel to receive care [7].

In conclusion, DPT was a successful intervention for clinical outcome measures (ODI, RMDQ, and NPRS), lower extremities muscle force, trunk mobility, activities of daily living (QUE), FMS, and quality of life (SF-12). Most importantly, DPT demonstrated more positive effects on cost-effectiveness, accessibility, and real-time feedback compared to CPT.

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Department sessions

Occupational Therapy				
13:30	Opening Remark	Prof. Minoru Hoshiyama	Nagoya	
Session Ⅰ				Presentation: 12 minutes Question & Answer: 5 minutes
13:35〜14:43	Chair	Prof. Ickpyo Hong	Yonsei	
13:35〜13:52		Suyeong Bae	Yonsei	Social participation and life satisfaction among adults with physical disabilities
13:52〜14:09		Yuga Takeda	Nagoya	Neural activity related to task shift/switching
14:09〜14:26		Yeonju Jin	Yonsei	Relationship between visual function of distance acuity, near acuity and contrast sensitivity and activities of daily living
14:26〜14:43		Masato Sasaki	Nagoya	Change of Brain Activity in Sensory Motor Cortex by Somatosensory Discrimination Task -A Preliminary Study
14:43〜15:00	Intermission			
Session Ⅱ				Presentation: 12 minutes Question & Answer: 5 minutes
15:00〜16:05	Chair	Prof. Minoru Hoshiyama	Nagoya	
15:00〜15:14		Prof. Yuko Nishiura	Nagoya	Development of automatic calendar App "yottey" for older persons with neurocognitive disorders
15:14〜15:31		Jung-Min Han	Yonsei	Health improving programs for older adults living alone: A systematic review
15:31〜15:48		Soo Yeon Yoo	Yonsei	Social Isolation Program for Older Adults Living Alone: A Systematic Literature Review
15:48〜16:05		Hyunseo An	Yonsei	Association Between Social Networks and Health Promoting Behaviors in Community Dwelling Older Adults
16:05〜	Closing Remark	Prof. Ickpyo Hong	Yonsei	

Social participation and life satisfaction among adults with physical disabilities

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Introduction

The number of adults having disabilities is rising in the Korea [1]. In Korea, 2.64 million people have disabilities, and 2.11 million are 50 years and older with diagnosed disabilities, with 49.4% having physical disabilities [1].

Older adults with disabilities experience more decline in physical and mental abilities than those without disabilities [2-3]. Physical disabilities often lead to limited social participation and impact their quality of life and life satisfaction [4-5].

Social participation can positively impact the life satisfaction of middle-aged individuals. Studies have shown that active social engagement reduces the anxiety and depression-related symptoms in middle-aged adults with no disabilities [6-7]. However, research on the connection between social participation and life satisfaction in middle-aged adults with disabilities remains unclear. Therefore, we aimed to investigate the association between social participation and the life satisfaction of middle-aged adults with disabilities.

Methods

This study utilized the 2016-2021 Korea Panel Survey of Employment for the Disabled (PSED) databases and conducted a retrospective cohort study. The dataset included demographic and clinical information of 4,577 Korean participants with disabilities. The final sample consisted of 558 middle-aged adults with physical disabilities.

Social participation was measured using a 4-point Likert scale (1 = "I can't partiwcipate at all," 2 = "I can't participate," 3 = "I tend to participate," 4 = "I participate a lot") and it was considered as the time-varying independent variable. The dependent variable was overall life satisfaction, assessed on a 5-point Likert scale (1 = strongly dissatisfied, 2 = dissatisfaction, 3 = neutral, 4 = satisfaction, 5 = strongly satisfied). Time-invariant covariates included age, gender, marital status, and educational attainment.

Latent growth models (LGMs) were employed to explore the relationship between life satisfaction and social participation over time (Figure 1) [8]. Model fit was assessed using five model fit indices.

The analysis revealed the association between time-varying social participation and life satisfaction, while controlling for time-invariant covariates. Data cleaning was performed in SAS (version 9.4), and LGM analysis was conducted using Mplus (version 8.8).

Results

Table 1 shows the demographic characteristics of adults with physical disabilities. Those who were satisfied with their lives numbered 1,411 (45.34%). The majority of the samples are females (n = 1,136, 80.51%).

Table. 1: The demographics of the participants (N = 558)

Variables	N (%)
Age, mean (SD)	57.39 ± 4.40
Sex	
Male	322 (57.71)
Female	236 (42.29)
Educational attainment	
Below middle school	306 (54.84)
High school	201 (36.02)
Above college	51 (9.14)
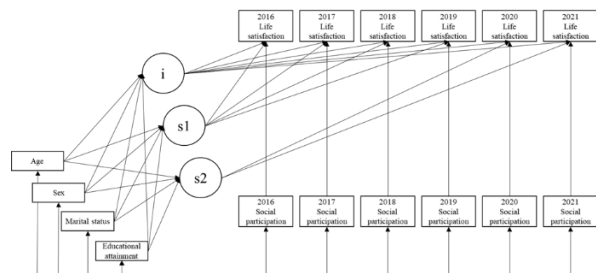
Figure. 1: The conceptual conditional piecewise growth analysis model

Table. 2: Association between social participation and life satisfaction from the conditional piecewise growth analysis model

Variable	Standardized coefficients
Time-varying covariates	
Social participation 2016	0.082*
Social participation 2017	0.131**
Social participation 2018	0.190**
Social participation 2019	0.268**
Social participation 2020	0.194**
Social participation 2021	0.137**

Note. *p<0.05; **p<0.01

The LGM model shows good model fit results, as indicated by a chi-square $\chi2$ value of 126.241 with a p-value of 0.000, an RMSEA (Root Mean Square Error of Approximation) of 0.049, a CFI (Comparative Fit Index) of 0.947, a TLI (Tucker-Lewis Index) of 0.927,

and an SRMR (Standardized Root Mean Square Residual) of 0.093 (Figure 1).

This LGM model revealed that social participation consistently had a positive association with life satisfaction across multiple time points, with standardized coefficients ranging from 0.082 to 0.268, all of which were statistically significant (all *p*-values < .05) (Table 2).

Discussions

This study investigated the association between social participation and life satisfaction in adults aged 50 to 64 with physical disabilities. The findings showed that a consistent and significant association between social participation and life satisfaction over time.

Social participation, which includes activities like cultural and religious leisure pursuits and interpersonal relationships, has been a focal point in prior research, particularly concerning individuals with disabilities [9]. Studies have emphasized their interest in participating both in the workforce and leisure activities, as it proves beneficial [10]. Nevertheless, individuals with disabilities have often been observed engaging in passive leisure activities like watching TV and listening to the radio [11-13]. These findings highlight the strong desire of individuals with disabilities to partake in social activities, both in terms of leisure and work, which can enhance their life satisfaction.

In a 2020 survey by the Korea Institute for Health and Social Affairs, disabled individuals cited economic challenges, poor health, and limited mobility as the main reasons for not participating in leisure activities [1, 14]. As middle-aged adults age, they have more time for leisure, but older adults with disabilities face increased limitations [15, 16]. Health policymakers should recognize these findings and create more accessible opportunities for disabled individuals to engage in leisure and social activities.

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Neural activity related to task shift/switching

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BACKGROUND: One of the therapeutic targets of occupational therapy is intervention for executive dysfunction. Patients with executive dysfunction show difficulty in starting, transitioning and switching consecutive tasks. When the human brain performs cognitive tasks, several brain regions are considered to form neural networks that functionally interrelate. Although some neural networks have been reported as large-scale networks that are constructed throughout the brain, the number of such networks, including large, small, and multiple overlapping networks, has not been clear. The activities of these neural networks are thought to interact with each other, and to alter from one network pattern to the next. However, the details of how this transition of network activity occurs are not clear. In the present study, I used magnetoencephalography and its analytical methods to clarify the shift/switching of task-related network mechanisms that are essential for continuity and change in behaviors.

(Heine et al., 2012)

METHODS: In the present study, I detected changes in brain activity that occurred during the time of task switching by continuously performing task switching with only a few instructions under the same stimulus environment. Subjects were asked to perform six active tasks in sequence every 30 seconds in response to information presented in an altruistic and continuous manner to visual, auditory, and somatosensory sensory information. The subjects were 12 healthy young adults. Brain activity was recorded using a magnetoencephalography (MEG), and cortical current density and estimated currents in the alpha frequency band of the brain region of interest (ROI) based on the current source were compared before and after the task conversion was taught cue. Brain activity during the task transformation was averaged and compared regardless of the task type.

RESULTS: Valid brain activity was obtained from 10 of the 12 subjects. The mean cortical current density before and after the task conversion cue was calculated, and six ROIs were defined based on the distribution of cortical current density before and after the cue ($p<0.05$, after FDR correction). The time course of activity in the alpha frequency band before and after the task conversion cue showed that the right insular cortex was more active before and after the cue, but the change over time in the right orbitofrontal cortex was not constant.
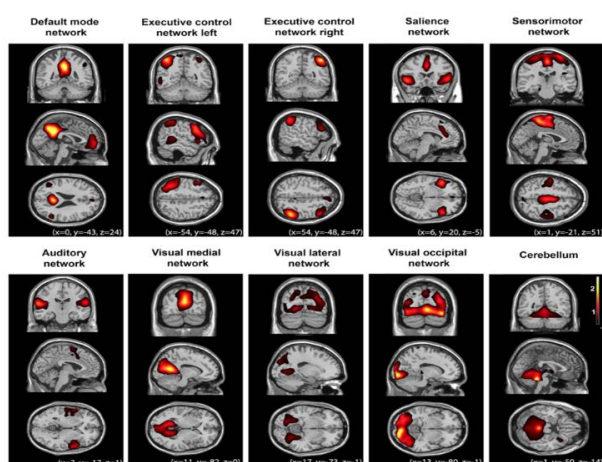
	P value	FDR corrected
caudal anterior cingulate R	0.072435632	0.10865345
caudal middle frontal R	0.058404032	0.10865345
frontal pole R	0.341559497	0.34155950
insula R	0.002082076	0.01249246
lateral orbito frontal R	0.015534148	0.04660244
temporal pole R	0.093660791	0.11239295

DISCUSSION: Brain activity during task switching was evaluated in the present study. By comparing the brain activity before and after the task switching, brain activity components related to the task switching was evaluated, regardless of whether the task was switched before or after the conversion. The brain regions that showed significant differences in task switching-related activity were the right insular cortex and the right lateral orbitofrontal cortex in terms of alpha frequency bandwidth. Both regions have been reported as brain regions related to task switching, but the insular cortex showed a clear time course of brain activity before and after task switching, suggesting that it was one of the brain regions that was prompted by external stimuli (cue) to task switching.

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Relationship between visual function of distance acuity, near acuity and contrast sensitivity and activities of daily living

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Introduction

Vision is an important sensory function for individuals to perform their daily activities independently [1]. Visual function is defined as how the eye functions, and it provides information about target locations and body movement as well as gives us the details that we need to see clearly [1]. This critical function declines with age which could lead to vision loss. As visual function decreases, older adults have more difficulties in activities of daily living. Older adults with impaired visual function experience a twofold increase in the risk of falls, along with an elevated risk of cognitive impairment, dementia, and a higher rate of comorbidity with other medical conditions [2]. Additionally, they exhibit a greater likelihood of concurrent physical and mental health conditions or complex comorbidities compared to the same age group [3]. Consequently, the decline in visual function among older adults is associated with increased difficulties in performing activities of daily living and participating in social engagements, contributing to negative health status.

Therefore, this study aimed to examine the relationship between visual function and independent activities of daily living in community-dwelling older adults.

Methods

We used a retrospective cross-sectional design. Out of the 3,817 participants in the 2021 National Health and Aging Trends Study (NHATS), 2,824 individuals were selected for the evaluation of visual function, excluding any missing data. We utilized a series of multivariate regression models and estimated the relationship between visual function and independent activities of daily living. We used the total scores of three visual function variables (distance acuity, near acuity, contrast sensitivity) as the independent variable and eight activities of daily living tasks (e.g., dressing, shopping) and total scores as the dependent variables. All statistical analyses and data management were conducted using SAS statistical software version 9.4 [4].

Results

The majority of the study sample was 75-79 years old ($n = 867$, 30.7%), and male ($n = 1,137$, 35.7%). Near acuity was statistically related to the total scores of the four basic activities of daily living (BADLs) ($\beta = 0.32$, standard error [SE] = 0.10; $p = 0.0018$), bathing ($\beta = 0.13$, SE = 0.05; $p = 0.0056$), eating ($\beta = 0.07$, SE = 0.03; $p = 0.0066$). However, distance acuity showed no significant relation to any of the BADLs activities. Contrast sensitivity was only negatively related to the eating item ($\beta = -0.06$, SE = 0.02; $p = 0.0048$) (Table 1). Near acuity was statistically related to four instrumental activities of daily living (IADLs) total scores ($\beta = 1.18$, SE = 0.27; $p = <.0001$), shopping ($\beta = 0.52$, SE = 0.10; $p = <.0001$), making hot meals ($\beta = 0.21$, SE = 0.10; $p = 0.0258$), and baking ($\beta = 0.32$, SE = 0.10; $p = 0.0020$). However, distance acuity showed no significant relation to any of the IADLs activities. Contrast sensitivity was only negatively related to the banking item ($\beta = -0.22$, SE = 0.08; $p = 0.0064$) (Table 2).

Table1. Multivariable linear regression models with vision function and BADLs in the older adults

Variable	Total score	p	Dressing	p	Toileting	p
Near acuity	0.32 (0.10)	<.00*	0.08 (0.05)	0.08	0.03 (0.03)	0.30
Distance acuity	0.04 (0.11)	0.73	0.01 (0.05)	0.76	0.01 (0.04)	0.84
Contrast sensitivity	-0.12 (0.08)	0.12	-0.03 (0.04)	0.40	-0.02 (0.03)	0.53

Note. *Significant at <.05.

Table1. Multivariable linear regression models with vision function and BADLs in the older adults (*cont.*)

Variable	Bathing	p	Eating	p
Near acuity	0.13 (0.05)	<.00*	0.07 (0.03)	<.00*
Distance acuity	-0.02 (0.05)	0.65	0.04 (0.03)	0.18
Contrast sensitivity	-0.02 (0.04)	0.63	-0.06 (0.02)	<.00*

Note. *Significant at <.05.

Table2. Multivariable linear regression models with vision function and IADLs in the older adults

Variable	Total score	p	Laun dry	p	Shop ping	p
Near acuity	1.18 (0.27)	<.00*	0.13 (0.10)	0.17	0.52 (0.10)	<.00*
Distance acuity	0.31 (0.29)	0.28	0.09 (0.11)	0.40	-0.02 (0.11)	0.84
Contrast sensitivity	-0.14 (0.21)	0.48	0.02 (0.08)	0.80	-0.02 (0.08)	0.78

Note. *Significant at <.05.

Table2. Multivariable linear regression models with vision function and IADLs in the older adults (*cont.*)

Variable	Making hot meals	p	Banking	p
Near acuity	0.21 (0.10)	<.02*	0.32 (0.10)	<.00*
Distance acuity	0.05 (0.10)	0.64	0.19 (0.11)	0.07
Contrast sensitivity	0.07 (0.07)	0.31	-0.22 (0.08)	<.00*

Note. *Significant at <.05.

Discussion

This study examined the relationship between visual function and independent activities of daily living and in community-dwelling older adults.

Our findings are consistent with previous studies, which suggest that good near acuity is related to older adults being independent in activities of daily living [5-7]. However, contrast sensitivity showed a negative relationship with eating and banking tasks. Older adults need longer stimulation durations due to delays in visual processing speed due to problems such as decline in cognitive function [1]. These results are limited because we do not know if strategies such as lighting was used when individuals were participating in activities of daily living. Distance vision was not significant in all activities of daily living. This is consistent with other studies showing nonsignificant associations between distance vision and activities of daily living tasks [8]. This means that distance vision may be less important or utilized less frequently than other visual function in performing activities of daily living. Near vision was the more frequently used visual function in various activities of daily living [5].

A limitation of this study was that it was difficult to determine the cause of visual function decline. Specifically, we were unable to ascertain whether the study subjects had any degenerative conditions related to vision (e.g., glaucoma, optic neuropathy, etc.). In this dataset, visual function was assessed in a large sample, potentially introducing measurement errors in the evaluation due to variances among evaluators (interviewers) and variations in the home environment.

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Change of Brain Activity in Sensory-Motor Cortex by Somatosensory Discrimination Task - A Preliminary Study –

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Introduction

Somatosensory loss is observed in approximately half of all stroke survivors [1]. Somatosensory loss in stroke survivors have a negative impact on their quality of life and personal safety, including impaired ability to perform daily tasks such as object recognition, grasping, and manipulation; balance during upright posture and walking; and risk of burns and injuries due to impaired warmth and pain perception [2].

Somatosensory discrimination training (SENSe assess) has been proposed for somatosensory loss after stroke, with the main goal of restoring somatosensory discrimination ability [2]. This training was developed by Carey et al. (2011) and is believed to provide higher functional recovery than conventional treatment methods [2].

Regarding to brain function, it has been reported that the human brain is constantly changing in a plastic manner in response to internal and external stimuli [2]. Focusing on this brain plasticity, training methods that aim to induce neuroplastic changes in brain regions related to somatosensory function are believed to provide higher functional recovery than conventional treatment methods [2]. However, the effects of the wrist position sense task on brain activity have not been studied neurophysiologically. Therefore, the purpose of this study was to clarify the changes in brain activity in the sensorimotor cortex induced by the Wrist Position Sense Test (WPST) included in SENSe using the magnetoencephalography (MEG). We think that clarifying these changes will provide basic insight into the effects of sensory functional-training on brain function.

Method

Thirteen healthy adult volunteers (10 males, average age: 22.8±1.6) participated in the experiment. All participants were right-handed and had no history of neurodegenerative diseases or organic brain disorders presenting as visual, auditory, or somatosensory impairments. Before the experiment, all participants were informed about the study and consent was obtained in writing. People with metal insertions in the body were excluded. This study was approved by ethical committee of Nagoya University, school of health science (approve number: 21-605).

The experiment task was the WPST [2]. First, the examiner fixed the participant's right wrist and forearm to hand splint in a position not visible to the participant, with the wrist in its natural position and the elbow bent at 90 degrees. Second, the examiner moved the patient`s wrist sequentially to several pre-determined angles. Participants answered the angle of their wrist by moving the pointer or verbally. After each trial, tester provided feedback to the participant on the correct angle.

The control task only consisted of the examiner to move the participant's right wrist, similar with experimental task, while the participant watched a silent film. Participants did not respond without being aware of the angle.

The experimental and control tasks were randomly administered to the same participants with at least a one-week interval between two tasks. The duration of two tasks was 20 minutes, respectively.

We recorded the resting-state brain activity before and after the task. Participant lay down on a bed in a magnetically shielded room and looked at cross mark projected on the monitor 30 cm ahead of participants during the recording. We used a whole-head MEG system (PQ1160C. RICHO) with 160 channels. The bandpass filter was between 0.3 to 200 Hz, at a sampling rate of 1000 Hz. We recorded the resting-state brain activity for 4 minutes in a dark room before and after the task. Before the MEG measurement of each participant, the shape of the scalp was measured using a 3D digitizer. Electrooculogram (EOG) and Electrocardiogram (ECG) were simultaneously recorded for artefact rejection. Participants were informed to keep their eyes open and not to sleep.

The MEG data were analyzed by 'Brainstorm' software (https://neuroimage.usc.edu/brainstorm). The EOG and ECG data were used to reject the artefacts caused by heart rate and eye movement.

Source data were generated for each of the experimental and control tasks. The power spectral density (PSD) was then calculated from the source data. MEG data were analyzed in the alpha band (8~12Hz). The difference in pre- and post-task brain activity (Δpost-pre) was then calculated by subtracting the pre-task PSD from the post-task PSD. The Δpost-pre was then compared between experimental and control tasks by permutation t-test. The significance level was set at 5%. In this study, we focused on the primary and secondary somatosensory area.

Results

Comparing the experimental and control tasks for sensory and motor cortex, the experimental task enhanced brain activity in the alpha frequency bands.

For the alpha band in the right hemisphere, the experimental task enhanced brain activity of the prefrontal, precentral, postcentral and superiorparietal compared to the control task (Fig.1). Additionally, in the left hemisphere alpha band, the experimental task enhanced brain activity in the prefrontal, precentral, and postcentral (Fig.1).
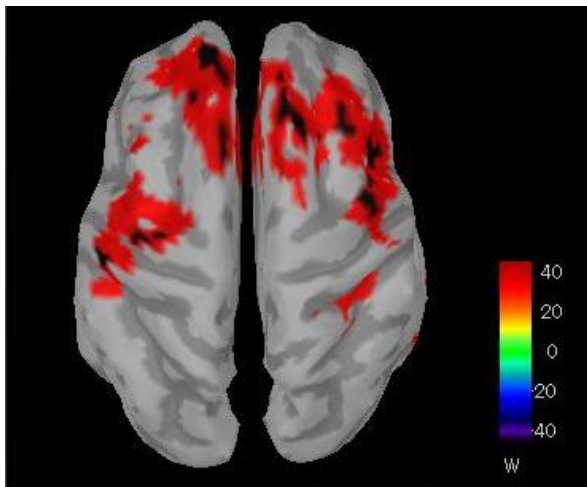

Fig.1 Significant differences in brain changes between experimental and control groups. The warm colors represent greater change in the experimental compared to the control taskgroup.

Discussion

In the alpha band, significant differences were found in the pre- and post-central. In the areas, power increased in the experimental task and slightly decreased in the control task. Previous studies showed that alpha power values increased linearly with increasing memory load in a working memory task [3]. In this studies, an increase in the alpha band source near the sensorimotor cortex was observed. This study also raised the hypothesis that the increase in alpha power may represent a neuronal mechanism for the maintenance of working memory. We thought that working memory was required during responding to the task based on the feedback from previous execution. The increase in alpha power during the task might continue to occur in the sensorimotor cortex after the task.

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Health improving programs for older adults living alone: A systematic review

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Introduction

As of 2022, the proportion of older adult living alone among 65 years or older population is 20.8% and it is reported that this will gradually increase. Compared to older adults who live with others, living alone have less social interaction, having lower awareness of health-related services, and show reduced levels of physical health, mental health, and social health as causes of high levels of depression, anxiety and loneliness [1].

It has been reported that all health factors are according to the reduced health level of older adults living alone because physical, mental, and social health have been reported to be interrelated [2]. Compared to older adults living with others, living alone have been reported to have a negative impact on not only their social health but also their physical and mental health due to the problem of social isolation [3]. Therefore, interest and necessity are being emphasized in terms of physical, mental, and social health of older adults living alone [4].

Therefore, health improving intervention for older adults living alone are necessary for their health and quality of life. This study aims to find the program method which brings most positive effects for physical, mental, and social health.

Methods

The database for this study was searched using PubMed, Embase, Riss, and DBpia. The search period was set from January 2013 to January 2023. Ant the main search terms are ('elderly' or 'older' or "old adult" or 'age') and ("health improve" or "health promotion") and ("living alone" or "live alone") and 'intervention'.

Eligible criteria for this research was 1) participation ages more than 65 who lives alone, 2) A study which related with health improving program, 3) Experimental group and control group design study, 4) Article available to watch full text, and 5) article which language's written in Korean or English. And exclude criteria for this research was 1) Dissertations, books, and protocol studies, 2) Conference presentation materials and posters.

A final 1,045 papers were searched. After reading titles, abstract, and full text, irrelevant literature was removed, and total 6 papers were selected.

Results

A total of 6 analysed studies were assigned and experimental and control group. All of the experimental groups were treated with a health promotion intervention, and the control group was provided with a previously applied nutritional intervention 1studies [5]. In the other 5 studies, no interventions were applied to the control group. As a result of confirming the intervention methods used in this study, the study conducted in Korean nursing conducted the most diverse program [3, 5, 6]. The intervention method was carried out in three ways: health care education, exercise program, and cognitive program for the experimental group. 2 Studies progressed home visit intervention [5, 6], and 1 study used agency visit intervention [3]. Looking at the remaining intervention methods, a study conducted only an exercise program though a home visit intervention [7], a study in which a medical alert device was worn through a tele intervention [8], nutrition education and eating habits management intervention was conducted through a combination of home visit intervention and tele intervention [9].

In the studies effects which had both tele and home visit intervention, experiment groups had improved their physical health, but didn't saw significant difference compare with control groups. Experiment groups mental health had improved but didn't saw significant difference [7]. And result about social health was not reported. In the studies effects which had used home visit intervention, physical health and mental health has showed improvement and significant difference. And in one study which showed social health results showed improvement and significant difference too.

Discussion

The purpose of this study was to conduct a systematic review focusing on the methods and effects of health promotion interventions for older adults living alone. The effectiveness of health promotion interventions showed significant difference according to two studies that conducted various health management education, exercise programs, and cognitive programs in nursing through home visit interventions [5, 6]. Additionally, one study reporting the effect on social health showed a significant difference [5]. Additionally, existing research reports that intervention methods that carry out the most diverse intervention activities show the most positive effects [10].

Table. 1: Intervention Type and Method

Intervention type [reference]	Intervention method
Visit/ tele [7]	Recommend Exercise from WHO (eg, Take a Walk for 30 Minute, Chair Stand Exercise, Stair Climbing, Sit-Ups)
Tele [8]	Using Medical Alert Device/Service and Receive Small Call Button
Visit/tele [9]	Visit Group: Home Visit to Check Eating Habits /Recommend Meals Tele Group: Telephone to Check Eating Habits
Visit [6]	Health Education (eg, Management of Chronic Disease, Fall-Prevention, Preparing for the Heat Wave, Food Positioning Prevention) Exercise Program (eg, Floor-Seated Exercise) Cognitive Function Stimulation Practice (eg, Drawing, Puzzle Matching, Hand-Knitting)
Agency [3]	Metabolic Syndrome Education (eg, Understanding Metabolic Syndrome, Preventing Metabolic Syndrome) Exercise Program (eg, Warm-up Exercise, Main Exercise, Cooling Down Exercise) Self-Esteem Promotion Strategy (eg, Caring Back Massage, Blessing Each Other, Accepting Each Other)
Visit [5]	Health Education: (Nutrition Education by Cooking Classes Focused on Healthy Foods and Convenient Recipes) Exercise Program: (eg, TheraBands Exercise, Aerobic Movements, Rhythmic Movement) Cognitive Program: (Calendar Making with Various Material, Cup Nanta by Rhythm)

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Social Isolation Program for Older Adults Living Alone: A Systematic Literature Review

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Introduction

With the development of the economy and medical technology, human lifespan has gradually increased, and Korean society has also entered an aging era. Looking at the proportion of single-person households by age group, those in their 60s were 16.4% and those in their 70s or older were 18.1% [1]. For men in their 60s, 14.5% and 18.3% for women were single-person households, and for men over 70, 8.8% and 27.3% of women were single-person households [1].

Old age is a time when social isolation is at high-risk, and one of the various causes of social isolation in old age is the increase in the number of elderly people living alone [2]. Social isolation has a negative impact on older people, leading them to a fractured form of life, causing deterioration in health, and even leading to suicide or lonely death [3].

Seniors living alone who complain of social isolation need appropriate intervention, and domestic research on this topic is lacking. Therefore, the purpose of this study is to confirm the need for intervention for seniors living alone who feel socially isolated through systematic review, and to summarize and consider the effectiveness of interventions for social isolation of seniors living alone.

Methods

The databases used in this study are RISS, CINAHL, SCOPUS, and Web of Science. We searched for papers published from January 1, 2012 to January 31, 2023. And the main search terms were "social isolation" AND (older OR elder OR aged OR geriatric) AND ("living alone" OR "live alone") AND intervention.

The selection criteria were 1) literature targeting seniors aged 60 or older living alone, 2) literature on intervention for social isolation, and 3) literature published from January 1, 2012 to January 31, 2023. And the exclusion criteria were 1) duplicate literature, 2) literature for which the full text could not be obtained, 3) literature written in languages other than Korean and English, and 4) systematic review literature.

A total of 2,962 papers were searched. After excluding duplicate literature and reading the abstract and full text, 5 papers were finally selected.

Results

In five studies, the subjects were all elderly people who complained of social isolation. As a result of analyzing the search results, the study subjects were classified into senior citizens living alone and senior citizens who did not live alone. Of the five studies, two (40%) only targeted elderly people living alone. The remaining three articles (60%) targeted elderly people living alone and non-alone elderly people.

To evaluate social isolation, the UCLA Loneliness Scale, Friendship Scale, LSNS-6, and DUFSS were used, and loneliness, depression, cognition, and quality of life were also evaluated.

Among the 5 studies, 4 studies compared groups that received intervention related to social isolation with groups that did not, and the remaining study conducted pre- and post-surveys on 21 subjects and compared the results [4- 8]. The period during which the intervention was provided varied from 8 weeks to 1 year and 9 months, and the number of interventions varied depending on the study, with a minimum of 5 times and a maximum of 70 times per week. There were four main types of interventions: discretionary activity interventions in the community, group activities and counseling interventions, interventions to learn how to use tablets and the Internet, and interventions related to social interaction such as telephone and in-person interventions [4-8].

The interventions provided in all five studies showed significant effects in reducing social isolation and loneliness. In addition, the effects of increased life satisfaction, increased social support, improved environmental quality of life, improved technical knowledge, well-being, and improved trust in people and public social security were also observed. Among these, environmental quality of life, trust in people and public social security, and technical literacy improved, but no significant effects were observed.

Table. 1: Details of the Intervention

| Authors (year) | Intervention | |
	EG	CON
Czaja et al. (2018) [4]	PRISM software applications	A notebook with printed content similar to that within PRISM
Gadbois et al. (2022) [5]	Learn how to use tablets, access the Internet, and participate in phone and Internet-based virtual senior center programs	-
Hernández -Ascanio et al. (2023) [6]	Intervention of six home-facing sessions and five phone calls sessions	Only a follow-up of the situation
Ristolainen et al. (2020) [7]	Consultation and activities including visits, outdoor gatherings, group exercises, and recreation	-
Winstead et al. (2014) [8]	Discretionary activities	-

Discussion

The purpose of this study was to analyze the effectiveness of interventions provided to elderly people living alone who are experiencing social isolation. First, the interventions provided in 4 of the 5 studies were interventions related to social relationships or interactions. In addition, there were computer-based arbitrations, but they only accounted for 1 out of 5 cases. Second, among the 5 studies, 3 evaluated quality of life. This means that there is a close relationship between social isolation and quality of life. Lastly, 3 of the 5 studies commonly evaluated social isolation and loneliness. This means that social isolation and loneliness are closely related and are an interactive relationship [9].

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Association Between Social Networks and Health Promoting Behaviors in Community-Dwelling Older Adults

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Introduction

As the period of old age extends, it becomes vital to live healthily and actively. The World Health Organization highlights the importance of health-promoting behaviors such as good eating habits and regular exercise [1].

Health-promoting behaviors are everyday actions that enhance overall well-being, particularly in older adults, and are influenced by personal and societal factors [2, 3]. Social networks refer to a specific set of connections between a limited number of people [4]. Social networks, which encompass relationships with family, friends, and others, play a crucial role in the health behaviors of older adults. Social networks have both structural (size, contact frequency) and functional (quality, support) aspects, each impacting health in different ways [5].

Current research on how these network aspects influence health-promoting behaviors in older adults is limited. This study aims to bridge this gap by analyzing the relationship between older adults' social networks and their health behaviors, especially in health management.

Methods

This research aimed to study the influence of social networks on the health behaviors of community-dwelling elderly individuals aged 65 and up. Conducted on April 18-19, 2023, the online survey had 226 participants. Data collection proceeded after the approval of the Yonsei University Institutional Review Board (IRB).

This study used the Korean version of the Lubben Social Network Scale (LSNS-18) to survey older adults' social networks [6]. LSNS-18 measures the social network size, contact frequency, and perceived social support in the family (relatives), neighbors, and friend networks. This research differentiated between non-cohabiting family and close relatives, thus investigating four networks: non-cohabiting family, relatives, neighbors, and friends. The scale used had 28 items, with seven items for each network.

The Korean version of the Health Enhancement Lifestyle Profile (K-HELP) was used to assess health-promoting behaviors, covering seven health-related areas [7]. A higher score on this tool reflected better health behaviors. The reliability of the tool in this study was Cronbach's $\alpha = .85$.

Data was analyzed with SAS 9.4, examining participants' demographics, social networks, and health behaviors using descriptive statistics. Health behavior differences were assessed via t-test, ANOVA, and Scheffe test. The correlation between social networks and health behaviors was determined using the Pearson correlation coefficient, and their relationship was further explored through hierarchical regression analysis.

Results

The study involved participants averaging 67.86 years old, with a majority being male. Most had a university degree or higher. Participants typically rated their economic and health statuses as average. Fewer reported depression, with an average PHQ-9 score of 3.67. Over half had chronic diseases, averaging 1.49 diseases each. Women with better economic or health statuses and non-depressed participants showed significantly higher health-promoting behaviors.

For the structural characteristics of social networks, the order of network size was friends, non-cohabiting family, relatives, and neighbors. Contact frequency was highest with non-cohabiting family, followed by friends, relatives, and neighbors. For functional characteristics, perceived social support was highest with non-cohabiting family, friends, relatives, and neighbors. The total health-promoting behavior score was 109.80±23.58. Among the seven sub-areas, scores were highest for activities of daily living, followed by diet, other health promotion and risk behaviors, stress management and spiritual participation, exercise, leisure, and productive/social activities.

Analysis between social networks and health-promoting behaviors showed significant positive correlations with all social network variables used in this study, as shown in Table 1.

Table. 1: Correlation between social networks and health-promoting behaviors

Variable		r (p)
		Health-promoting behaviors
Network size	Non-cohabiting family	0.299***
	Relatives	0.323***
	Friend	0.256***
	Neighbor	0.345***
Contact frequency	Non-cohabiting family	0.249***
	Relatives	0.308***
	Friend	0.257***
	Neighbor	0.356***
Social support	Non-cohabiting family	0.440***
	Relatives	0.454***
	Friend	0.435***
	Neighbor	0.478***

*p<.05, **p<.01, ***p<.001.

In the study, hierarchical regression analysis was conducted to evaluate the impact of social networks on health-promoting behaviors (HPB), as shown in Table 2.

Three models were developed: Model 1 utilized demographics as control variables, Model 2 added structural aspects of social networks, and Model 3 incorporated functional aspects. In Model 1, gender, subjective economic status, and depression statistically significantly correlated with HPB. In Model 2, gender, subjective economic status, depression, relative network size, and neighbor contact frequency correlated significantly with HPB. In Model 3, gender, depression, and social support from neighbors showed significant correlations with HPB. The changes in explanatory power between each model were significant.

Table. 2: Influencing factors on health-promoting behaviors

Variable		Model 1	Model 2	Model 3
		β	β	β
Gender (ref=female)		0.19**	0.15*	0.12*
Subjective economic status		0.17**	0.14*	0.09
Subjective health status		0.12	0.09	0.10
Depression		-0.26***	-0.21**	-0.19**
Network size	Non-cohabiting family		0.03	-0.04
	Relatives		0.17*	0.06
	Friend		0.06	0.01
	Neighbor		0.01	-0.08
Contact frequency	Non- cohabiting family		0.02	-0.01
	Relatives		0.07	0.05
	Friend		-0.04	-0.09
	Neighbor		0.21*	0.07
Social support	Non- cohabiting family			0.09
	Relatives			0.10
	Friend			0.12
	Neighbor			0.27**
R^2(Adjusted R^2)		.217 (.202)	.348 (.311)	.415 (.370)
F		15.28***	9.45***	9.26**

*p<.05, **p<.01, ***p<.001. ref = Reference group.

Discussions

This study examined the influence of social networks' structural and functional aspects on the health-promoting behaviors of elderly residents in a community. Social networks showed significant positive correlations with health-promoting behaviors, and the primary influencing factor of health-promoting behaviors was social support from neighbors. Establishing and activating satisfying social networks among older adults in the community is deemed essential to promote health-promoting behaviors. Encouraging mutual support for health-promoting actions and active participation in healthcare tasks is also considered crucial. When implementing lifestyle intervention programs for older adults, leveraging social support through these social networks is expected to produce synergistic effects.

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