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Original Article

A comparative analysis of attitudes toward stem cell research and regenerative medicine between six countries — A pilot study

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A R T I C L E   I N F O

A B S T R A C T

Introduction: Breakthroughs in stem cell research (SCR) and regenerative medicine (RM) have attracted significant public attention worldwide. Simultaneously, scientific communities and science policies have tried to establish appropriate governance of SCR and RM. In this context, effective communication between scientific communities and the public is regarded as a key factor. However, the diversity of public attitudes and interests has not been sufficiently examined, especially the differences across countries.
Methods: We conducted an international comparison of public attitudes toward SCR and RM. We circulated an internet questionnaire among people in six countries: Japan, South Korea, the United States, the UK, Germany, and France. We collected 100 valid responses from each country, and a total of 600 responses were obtained.
Results: Our key findings are the diversity of interests in RM, which can be expressed as user pragmatism, governance and handling of RM, risk, and benefit, and scientific interests. The priority of interests varied across the six countries, and the variations may be influenced by the political, social, cultural, and media contexts of SCR and RM in each country.
Conclusion: The implications can contribute to a deeper understanding of the diversity of public attitudes, and bring about an appropriate examination of a wide range of ethical and social concerns of SCR and RM in global contexts.

1. Introduction

Breakthroughs in stem cell research (SCR) and regenerative medicine (RM), such as embryonic stem cells (ESCs) [1] and induced pluripotent stem cells (iPSCs) [2—4], have attracted widespread public attention.

Every country started active discussions on funding system and regulations for SCR and RM, including Japan. The Japanese Ministry of Education, Sports, Culture, Science, and Technology (MEXT) and related agencies such as Japan Science and Technology Agency (JST) funded to promote the research and development of SCR and RM. In the history of their funding, they supported not only research of iPSCs but also of other kinds of stem cells [5]. In addition, current policy documents often emphasize the importance and value of innovation in SCR and RM [6,7]. The Japanese authorities have also changed regulatory frameworks for SCR and RM. In 2013, laws concerning SCR and RM changed; the Act on the Promotion of Regenerative Medicine and the Act on the Safety of Regenerative Medicine was enacted, and the Pharmaceutical and Medical Device Act was revised and renamed to the Pharmaceuticals, Medical Devices and Other Therapeutic Products Act [8]. The three acts are

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collectively known as the "Regenerative Medicine Three Acts." These regulatory frameworks were implemented following legal actions, such as those involving the administration of stem cells without sufficient examination of safety and effectiveness [9].

Public attention in SCR and RM has also been examined in the context of increased anticipation of SCR and RM. For example, in Japan, after the human iPSCs were established by Dr. Shinya Yamanaka's research group in 2007, news regarding research on iPSCs and iPSC-derived products captured media attention [10]. The increase in the amount of media discourses brought public anticipation and high recognition of keywords such as iPSCs and RM [11]. Previous studies have found optimism and peripheralization of ethical, legal, and social issues (ELSI) in the media sphere [10,12,13]. Issues related to the hype concerning iPSC and RM have also been highlighted.

Considering the contexts of public interests and requests for the management of the hype of SCR and RM, academic societies have actively discussed social aspects and perspectives for governance. For example, the International Society for Stem Cell Research (ISSCR) published *the ISSCR Guidelines for Stem Cell Research and Clinical Translation* in 2016 and recommended that the stem cell research community should promote "accurate, balanced, and responsive public representations" of SCR and RM. In addition, it emphasizes fundamental ethical principles [14]. More recently, in 2021, the ISSCR revised these guidelines. Fundamental ethical principles were revised and upgraded to "integrity of research enterprise," "primacy of patient/participant welfare," "respect for patients and research subjects," "transparency," and "social and distributive justice [15]."

In the global context of discussions on ELSI and science policies, perspectives appearing in ISSCR guidelines have often been considered, connecting to discussions on "Responsible Research and Innovation (RRI)." In the science and technology policy, the framework of "RRI" was suggested, specifically in the European framework Horizon 2020 [16]. The framework invites us to examine ELSI, upstream public engagement, and consider the inclusion of various stakeholders in modern innovative processes. Therefore, RRI has been expressed as "Responsible innovation means taking care of the future through collective stewardship of science and innovation in the present [17]."

To conduct RRI of emerging science and technology, including SCR and RM, it is essential to understand the diversity of public opinions. Previous studies in Japan found that public interest in SCR and RM was primarily related to the consequences of the potential success of RM, such as the cost of the new therapy, countermeasures for risks and accidents, and clarification of responsibility and liability, rather than in the scientific aspects. Although the public emphasized the pragmatic perspectives, the experts (members of the research community of SCR and RM) in RM focused on scientific content and validation, considering the current lack of clinical trials on RM [18]. In addition, Inoue et al. [19] showed the diversity of public opinions and their reservations on SCR and RM, particularly in the case of human-animal chimera studies. Although over 70% of respondents have positive and supportive attitudes towards the promotion of RM-related research, approximately half of the respondents had a negative attitude towards the generation of human-animal chimeras [19]. Sawai et al. [20] showed that information sharing increased the acceptance of human-animal chimeras, while one-third remained unacceptable.

Research that focused on public attitudes toward SCR have likewise been conducted in other countries. For example, Nisbet and Becker analyzed the public opinion polls on stem cells in the United States of America (USA). They found that the public have delicate moral senses toward embryonic stem cell, and particularly have strong reservations about research on the destruction of human embryo [21]. Nick Allum et al. Conducted an international comparison of the public opinion toward SCR between Europe, Canada, and the USA. They pointed out the effect of the sense of religion on the public ethics toward SCR. This tendency is more significant in the USA. On the other hand, the respondents in Europe and Canada regard the benefit to the society as a key driver for the support to SCR [22].

With the increase in anticipation of SCR and RM, communication considering the diversity of public opinions has become a prominent issue. It is essential to understand the nature of the topics that interest the public and the factors they consider important for the acceptance of SCR and RM. At the same time, we must consider the diversity of public attitudes across countries. Every political, cultural, social, ethical, and moral context seems to influence the public attitudes toward SCR and RM differently among countries. However, there is a lack of knowledge about the diversity of public interests in a global context. We conducted a questionnaire to compare the public attitudes toward SCR and RM in six countries: Japan, South Korea, the USA, the United Kingdom (UK), Germany, and France.

2. Methods

From 14th to 28th September 2018, we circulated a survey questionnaire among people in six countries: Japan, South Korea, the USA, the UK, Germany, and France. We collected 100 valid responses from each country. A total of 600 responses were obtained. The participants were recruited through Rakuten Insight ©. The number of participants was set the same for each age (from 20s to 60s) and gender (male or female). Additionally, we collected responses from those who graduated from universities (and some of them have master's or doctoral degrees), because we would like to make bias by educational background small. According to this background bias, the average family income is relatively high, compared to national statistics on income. The basic information of demography of responses are shown in supplemental data (see Supplement 1).

We designed multiple-choice questions to facilitate comparisons among the answers provided by the six countries. The key questions were as follows: "What do you want to know regarding RM?" "What factors are important for your acceptance of RM?" and "Which organs do you want to regenerate in RM therapy in the future?" Several questions were designed based on previous studies on public attitudes toward nuclear energy [23,24]. We had used the same questions in previous studies on public attitudes toward SCR and RM in Japan [18]. Table 1 shows a rough sample of the questionnaire. In the following analysis, we conducted a cross-table analysis and compared the differences between the answers of the six countries.

3. Results

3.1. The recognition of iPSCs and ESCs

Fig. 1 shows the recognition of keywords of iPSCs and ESCs in each country. The most significant feature of these results is the high recognition of iPSCs in Japan. Over 97% of the respondents answered, "I have heard of iPSCs." However, this trend has not been observed in other countries. The recognition of keywords of ESCs is more common in the other five countries as compared to the keywords of iPSCs.

Fig. 2 shows that a majority of respondents answered "I think we should press ahead with regenerative medicine research" or "I have a few concerns, but it is inevitable that regenerative medicine

Table 1
Basic structure of the questionnaires.

| Theme	The public	References on previous studies
Recognition of SCR & RM	Recognition of keywords on iPSCs & ESCs Opinion for promotion of RM research, Expected time of achievement of RM, Expected contents of RM after 10 years	Shineha et al. [10]; Shineha et al. [18]
Interest topics on SCR & RM	What do you want to know? What factors are important for your acceptance of RM?	Shineha et al. [18], Hayashi & Morikawa [23], Kitada & Hayashi [24]
Anticipation on SCR & RM	Which organs do you want to regenerate in RM therapy in the future? How much can you pay for the anticipated therapy?	–
Demography	Age, Gender, Education, Income, Religion, Expertise, etc.	
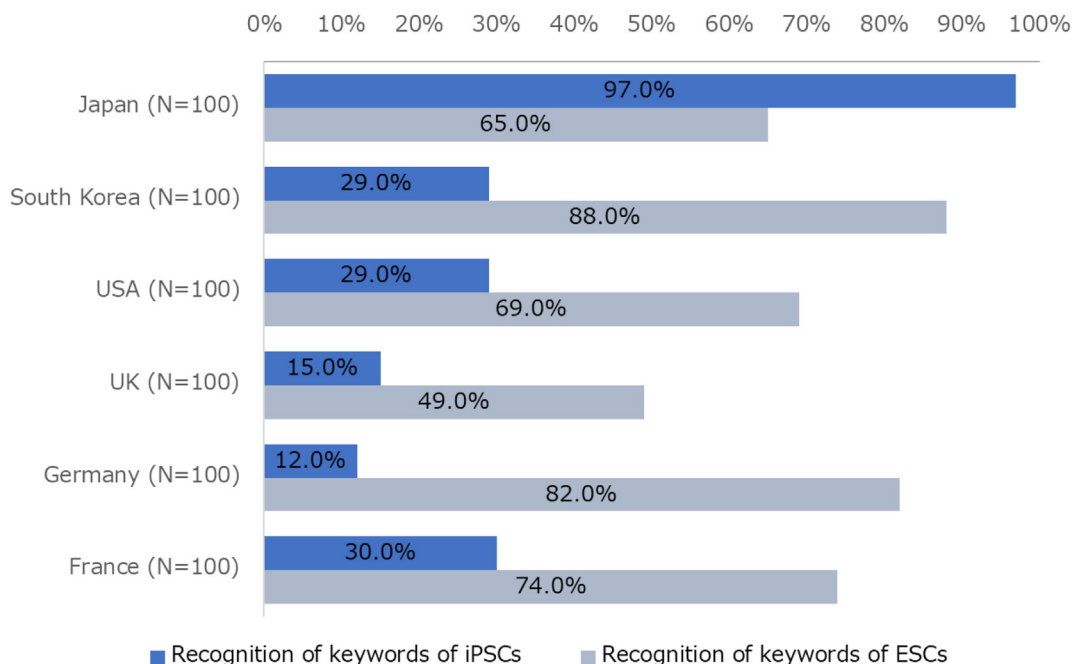
Fig. 1. Recognition of keywords of iPSCs and ESCs (Have you heard keywords of iPSCs and ESCs?).
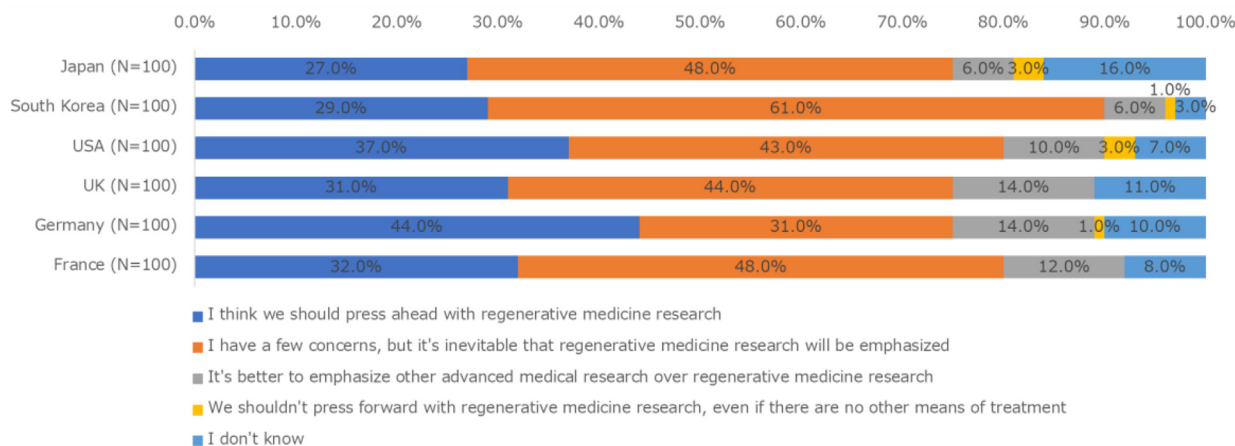

Fig. 2. Opinions concerning the progress of RM (Please select one statement from the following that best describes your overall thoughts about regenerative medicine research).

research will be emphasized." In other words, the majority agrees with the progress of SCR and RM.

However, we must consider the difference among the responses to questions focusing on trusting the experts. In this survey, we use the term "experts" as a general designation for scientists and researchers in RM. We asked, "Can you trust the story of experts on the safety and effects of RM?" In Japan and South Korea, the ratio of "agree" was low (Japan: 9.0%, South Korea: 6.0%), compared to the ratios in other four countries (USA: 27.0%, UK: 21.0%, Germany: 29.0%, France: 20.0%). Simultaneously, the response "I cannot decide" was high in Japan (41.0%) and South Korea (35.0%). In summary, the public may adopt a "wait and see" approach in these two countries.
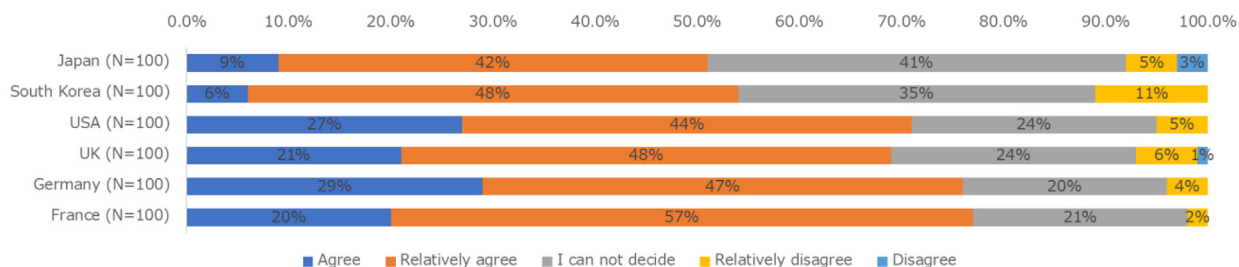
Fig. 3. Trust of experts' discourses (Can you trust the story of experts on the safety and effects of RM?).

3.2. Differences in interests among six countries

Interestingly, the topics that the public wants to know about vary across the six countries (Fig. 4). In this analysis, we conducted a chi-square test to determine their independence. Generally speaking, "risk" attracted public interest in each country. In five countries except for the USA, "risk" is the most interesting topic (France: 69.0%, Japan, UK, Germany: 61.0%, South Korea 51.0%). On the other hand, "benefit" is more interesting in the UK (56.0%), the USA (50.0%), France (48.0%), and Germany (42.0%), as compared to Japan (9.0%) and South Korea (29.0%). Specifically in the USA, "benefit" is garnered the most interest.

In Japan and South Korea, the trend of answers is different from that in other countries. The ratio of interesting topics of "cost of care" (Japan: 47.0%, South Korea: 44.0%), "measures for safety" (South Korea: 39.0%, Japan: 36.0%), and "responses to medical accidents" (Japan: 24.0%, South Korea: 21.0%) are higher than those in other countries. These topics are related to interest once RM is implemented in society. Among French respondents, "measures for safety" attracted their interests (36.0%).

"Mechanism of RM" is interesting in France (41.0%), Japan (38.0%), and USA (32.0%). The ratio of answers on "ethical issues" was marked from 16.0% to 27.0%, and here we did not find significant differences. The ratio of interest regarding other topics such as "industrial possibilities," "national policy or regulation," and "history of RM" is relatively low.

Fig. 5 shows the results of the factors considered important for the acceptance of RM. Respondents from Japan and South Korea regarded "whether experts can deal with risk and accidents" as the most important factors for their acceptance of RM (Japan: 61.0%, South Korea: 49.0%). In Japan, "clarification of responsibility and liability" was emphasized (35.0%), and the same was the case for Germany (36.0%).

Respondents from France and Germany regarded the "credibility of executors of research activities such as university, government, companies, and so on" as the most important factor for their acceptance (France: 51.0%, Germany: 40.0%).

Although the issue of "Whether society can prevent abuse and misuse by regulation" was very attractive in the UK (51%), this was an important factor in all countries. Respondents in the UK also
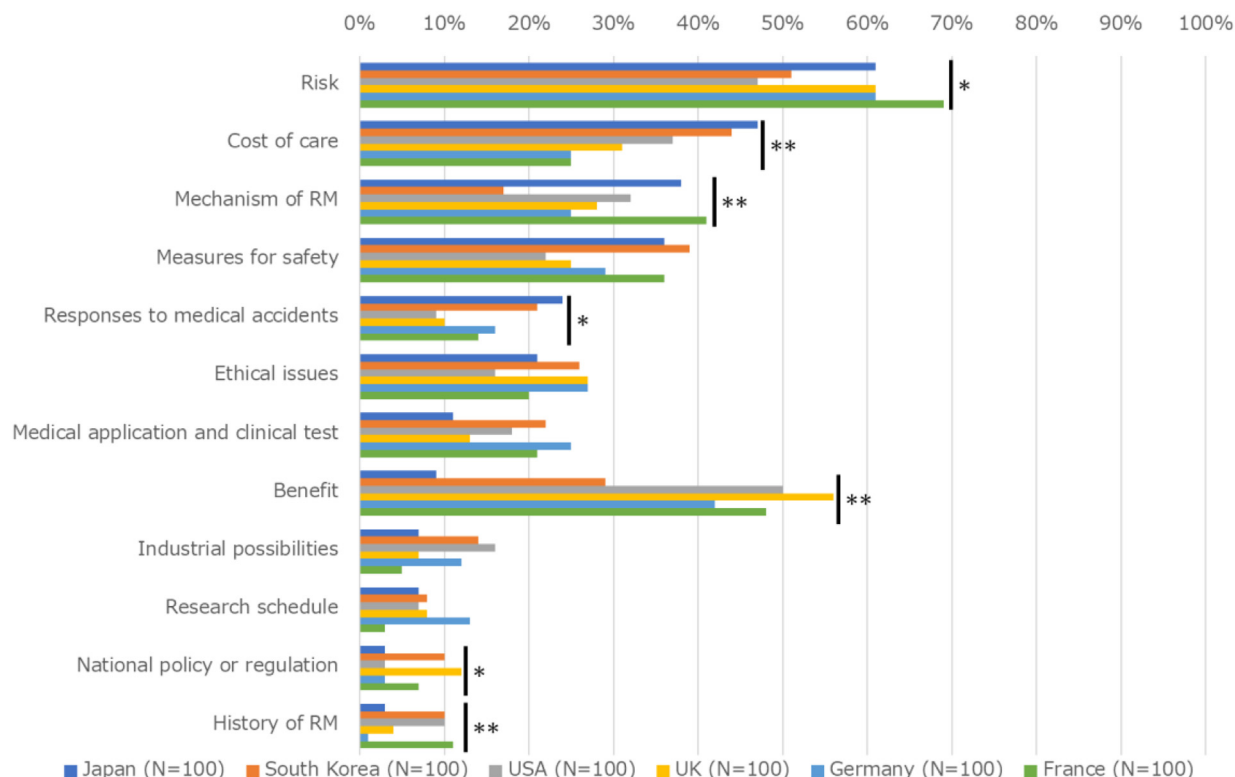

Fig. 4. Interested topics on RM (What do you want to know? Please choose three interesting topics.) A Chi-square test was conducted. *$p < 0.05$, **$p < 0.01$.
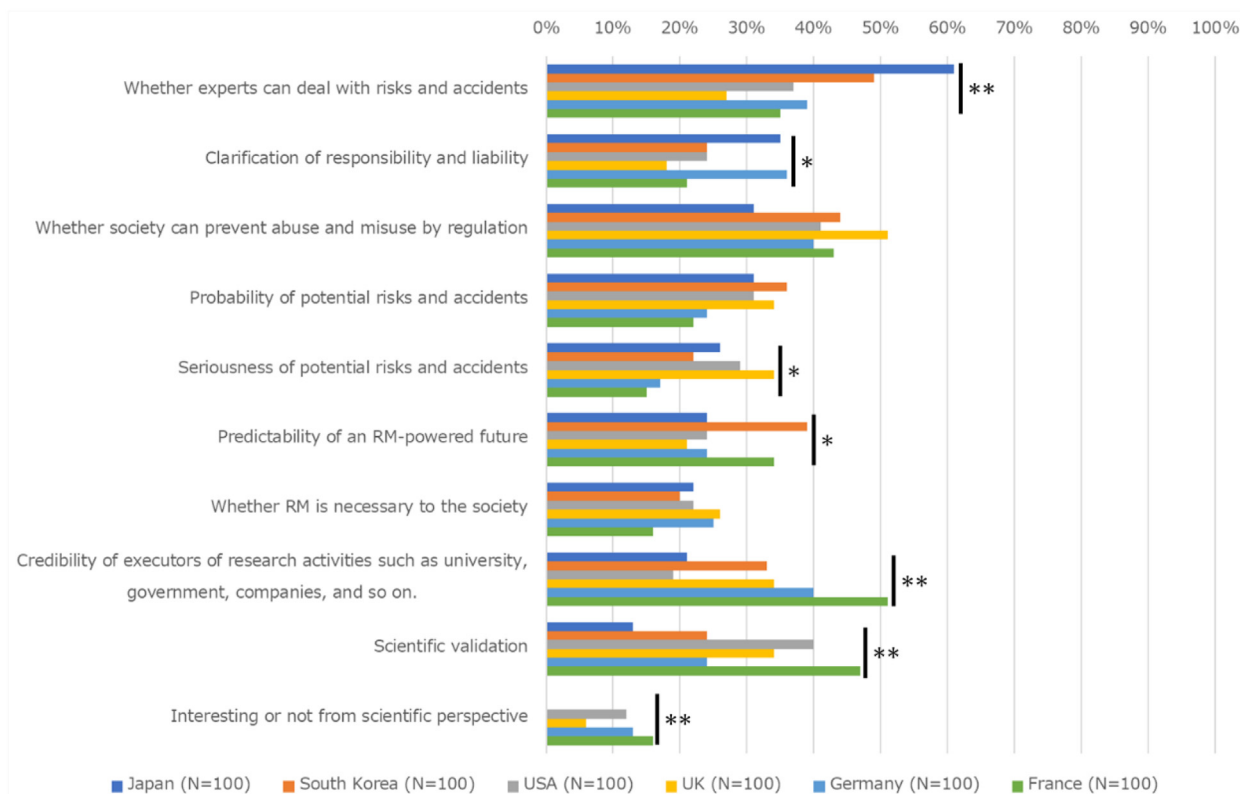
Fig. 5. What factors are important for your acceptance of regenerative medicine? Please choose three factors. Chi-square test was conducted. *$p < 0.05$, **$p < 0.01$.

answered "seriousness of potential risks and accidents" (34.0%), as compared to other countries. The focus on "scientific validation," was emphasized in France (47.0%), the USA (40.0%), and Germany (34.0%).

3.3. Differences of expected RM and sense of cost among six countries

We investigated the body part where the RM was expected to be utilized. The results are shown in Table 2, and we can find some differences in expected RM among the six countries.

The "Heart and Blood Vessels" and "Brain and Nervous System" are the usual expected parts for the application of regenerative medicine. The expectation of the application of RM in "Heart and Blood Vessels" came first in South Korea (53.0%), Germany (46.0%), and the UK (34.0%), and came second in Japan (41.0%) and France (49.0%). The expectation of the application of RM in the "Brain and Nervous System" came first in Japan (46.0%) and France (53.0%), and came second in South Korea (48.0%), Germany (38.0%), and the USA (29.0%).

In Japan, "Eyes" (35.0%) and "Teeth" (25.0%) were also considered, in contrast to other countries' responses. "Liver," "Muscle," and "Skin" were highly considered in the USA and UK. In Germany, "Bones" and "Blood" were relatively selected, as compared to other countries.

4. Discussion

Sheila Jasanoff discussed the importance to understand "civic epistemology," how the people think about science and the

Table 2
Differences of anticipated RM across six countries (Please select three parts of the body for which you expect regenerative medicine to be utilized).

Please select three parts of the body for which you expect regenerative medicine to be utilized.	Japan (N = 100)	South Korea (N = 100)	USA (N = 100)	UK (N = 100)	Germany (N = 100)	France (N = 100)
Skin	17.0%	26.0%	30.0%	27.0%	21.0%	23.0%
Bones	15.0%	19.0%	18.0%	19.0%	25.0%	15.0%
Cartilage	5.0%	17.0%	23.0%	20.0%	9.0%	15.0%
Eyes	35.0%	27.0%	22.0%	19.0%	18.0%	27.0%
Ears	3.0%	4.0%	9.0%	7.0%	4.0%	5.0%
The heart and blood vessels	41.0%	53.0%	28.0%	34.0%	46.0%	49.0%
The brain and nervous system	46.0%	48.0%	29.0%	23.0%	38.0%	53.0%
Teeth	25.0%	12.0%	10.0%	12.0%	14.0%	9.0%
Liver	13.0%	15.0%	23.0%	32.0%	18.0%	17.0%
Kidneys	10.0%	12.0%	28.0%	25.0%	18.0%	11.0%
The stomach and intestines	8.0%	16.0%	8.0%	7.0%	16.0%	17.0%
The blood	13.0%	15.0%	16.0%	20.0%	23.0%	21.0%
Hair	7.0%	19.0%	12.0%	10.0%	8.0%	10.0%
Muscles	7.0%	10.0%	26.0%	23.0%	17.0%	12.0%

collective knowledge on science, to consider the variety of science policies and regulatory systems of each country throughout her comparative analysis of science policies in the USA, UK, and Germany [25]. Understanding of civic epistemology of each country will give us valuable implications to discuss effective public engagement and communication between the scientific communities and the public.

Considering the discussion described above, our findings will contribute to a first step to understand the diversity of the public interests in a careful way. Although there are several trials on international comparison [21,22], there are no comparisons of six countries including Western and Asian countries. Furthermore, there is limited information on the diversity of interests in RM according to countries. Our presented data has some limitations such as small number of samples, it visualized that the diversity of interests in RM across the six countries. It seems that these interests can be of several types, such as user pragmatism, governance and handling of RM, risk, and benefit, and scientific interests. The types of interests are different across countries (Fig. 5), and these differences may be influenced by the political, social, cultural contexts of each country. Thus, we can step into the discussions on the next question. Why have such differences arisen? This question is not discussed in this article, but it will be a valuable theme in future research.

Another interesting finding is that the Japanese respondents marked a higher recognition of iPSC keywords than in other countries. In Japan, the number of news broadcasts has increased, particularly after the establishment of human iPSCs [9]. The media context has influenced the public attitudes toward RM. Media hype may also cultivate high anticipation regarding the social implementation of RM. In addition, the different contexts are rooted in the differences in the anticipation of body parts for RM utilization in the six countries (Table 2). For example, in Japan, clinical trials of iPSC-derived retinal pigment cells in patients with age-related macular degeneration have been conducted and reported repeatedly in mass media. In addition, Kamenova and Caufield [12] pointed out that a generally optimistic tone appeared in news articles analyzing clinical trials involving transplantation of neural precursor cells derived from embryonic stem cells for the treatment of spinal damage in the USA, UK, and Canada. For further research, the analysis of the correlation between the number of types of clinical tests and news articles may bear implications.

In Japan and South Korea, trust in the experts' testimonies regarding the safety of RM is relatively lower as compared to the other four countries (see Fig. 3). Both Japan and Korea experience big fabrication issues concerning SCR: cases of Hwang Woo-Suk and STAP cells. Media hype on these scandals seem to bring about high recognition of the keywords of iPSCs and ESCs in the two countries (Fig. 1). Trust has been pointed out as one of the most important factors for social acceptance and participation in emerging science and technology [18,26]. This point is related to the high interest of "governance and handling of RM." To cultivate trust between RM communities and the public, active information sharing is essential, while considering the differences in public interests in each country (see Figs. 4 and 5). Simultaneously, we should consider the difference in interests between the public and experts [18]. Previous studies in Japan showed that RM experts tend to focus on scientific content and validation, while the publics' interest in RM was primarily related to the consequences of the success of RM, such as the cost of care, countermeasures for risks and accidents, and clarification of responsibility and liability, rather than the scientific aspects.

For further research, it is necessary to examine the possibilities that these differences were influenced by the diversity of social and cultural characteristics of respondents between countries.

Although the evaluation of net effects of those social and cultural factors is a difficult challenge, Nick Allum and his colleagues conducted a comparative analysis of effects of knowledge and social and economic factors on the public attitudes toward biotechnology in European countries [27]. In another viewpoint, Johnson et al. tried to describe the relation between culture and responses [28]. These previous implications give us ways to think for future directions.

Here, we discuss the limitations of our data. The responses of this survey were collected through a web-based questionnaire and the participants were recruited through Rakuten Insight ©. The number of respondents was limited to 100 for each country. Hence, sampling biases could not be avoided. However, when we focus on the results of the responses from Japan, the presented data showed that the rank order of interested topics is basically similar to previous research [18]. Although there are minimal differences between the order on important factors for acceptance of RM, they are similar in that the factors concerning governance are regarded as a high priority. When we focused on the differences between the two research, we found that the rank of interested topics of "mechanism of RM" of the presented data are relatively higher than the previous one. Additionally, the rank of "credibility of executors of research activities such as university, government, companies, and so on" for acceptance of RM is different. These differences were influenced by the differences in the educational backgrounds of the respondents. As mentioned in the Methods section, this research focused on opinions of participants who graduated from university. Although the social meaning of academic degrees is different among the six countries according to their differences of histories, we guessed and expected that the effect of bias from the educational background will become small in our international comparison. Simultaneously, our respondents from each country tend to have a higher-than-average income according to their educational backgrounds.

Although we would like to avoid highlighting the statistical representativeness of our data, the presented data can be used as a rapid reference to roughly understand public attitudes toward SCR and RM across the six countries. For a continuous dialogue among stakeholders, we should consider not only differences of interests presented in this paper and previous studies [18] but also the hurdles in and measures toward encouraging the experts to communicate with the public. Time, opportunities, and evaluation systems for those communication activities were found to be important factors in encouraging the participation of experts in effective communications [29].

5. Conclusions

Our key findings are the diversity of interests in RM among the six countries. In addition, these interests can be categorized and expressed as user pragmatism, governance and handling of RM, risk, and benefit, and scientific interests. In addition, we focused on the status of recognition of keywords and the trust of experts in SCR and RM. These differences also vary with each country and may be influenced by the political, social, cultural, and media contexts of SCR and RM in each country.

The implications of this study can contribute to effective and upstream communication among stakeholders, which is the key factor for RRI in SCR and RM. A deeper understanding of the diversity of public attitudes and their background will facilitate the appropriate examination of a wide range of ethical and social concerns regarding SCR and RM while connecting to the fundamental ethical principles suggested by the ISSCR [13,14]. Discussions on communication activities concerning SCR and RM are anticipated to consider the diversity of interests in a global context.

Declaration of competing interest

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.reth.2022.04.007.

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