<table>
<thead>
<tr>
<th>Title</th>
<th>A surveillance study of the current status of reirradiation and patterns of practice</th>
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<tbody>
<tr>
<td>Author(s)</td>
<td>Yamazaki, Hideya; Fushiki, Masato; Mizowaki, Takashi; Kansai Cancer Therapist Group</td>
</tr>
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<td>Repository</td>
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</table>
A surveillance study of the current status of reirradiation and patterns of practice

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2Department of Radiation Oncology, Nagahama City Hospital, Nagahama, Shiga, Japan
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ABSTRACT

The aim of this study was to survey the current status of reirradiation (Re-RT) and patterns of practice in Japan. An email questionnaire was sent to Kansai Cancer Therapist Group partner institutions, using questions similar to those in the Canadian radiation oncologist (RO) survey (2008). A total of 34 ROs from 28 institutions returned the survey. All 28 institutions experienced Re-RT cases in 2014. However, 26 of the 28 institutions (93%) reported difficulty in obtaining Re-RT case information from their respective databases. Responses from 19 institutions included the number of Re-RT cases; this rose from 183 in the period 2005–2009 (institution median = 4; 2–12.9) to 562 in the period 2010–2014 (institution median = 26; 2–225). Important considerations for indication of Re-RT were age (65%), performance status (83%), life expectancy (70%), absence of distant metastases (67%), and interval since previous treatment (73%). Previous total radiation dose (48%), volume of tissue irradiated (72%), and the biologically equivalent dose (BED; 68.5%) were taken into account during Re-RT planning. These factors were similar to those considered in the Canadian survey; however, the present study did not consider age. In eight site-specific scenarios, barring central nervous system recurrence, more than 90% of ROs agreed to perform Re-RT, which was higher than the percentage observed in the Canadian survey. Re-RT cases have increased in number and aroused interest among ROs in this decade of advanced technology. However, consensus building to establish guidelines for the practice and prospective evaluation of Re-RT is required.

KEYWORDS: reirradiation, questionnaire

INTRODUCTION

The advancement of treatment modalities in surgery, chemotherapy and radiotherapy (RT) has improved survival rate and loco-regional control at many sites of cancer occurrence. However, in-field cancer recurrence after RT remains an obstacle to cure [1]. Treatment options for in-field cancer recurrence after RT include surgery, systemic chemotherapy, and reirradiation (Re-RT) [2–7]. With the advancement of modern radiation techniques, Re-RT has become a promising optional therapy that uses state-of-the-art advanced technologies, including intensity-modulated radiation therapy (IMRT), stereotactic RT (SRT), and particle therapy [5–10]. However, there is little evidence in support of Re-RT therapy; therefore, radiation oncologists (ROs) should make clinical decisions on their own experiences, either with palliative or radical intention. In other words, Re-RT is still in the experimental phase and requires further exploration. The objective of this study was to survey the present state of Re-RT and to determine its patterns of practice for in-field cancer recurrence after previous RT. In addition, we compared the present results with those of the Canadian survey to examine changes across decades and between countries [11].

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MATERIALS AND METHODS

A survey questionnaire (refer to supplement) was emailed to ROs registered in the Kansai Cancer Therapist Group directory as of 2015. At the time of correspondence, all the respondents were actively practicing in Japan. Part I of the survey questionnaire investigated the following: the actual number of Re-RT cases in 2014, 2005–2009 and 2010–2014, both in total and sub-grouped by location. Part II investigated the indications for Re-RT, Re-RT treatment planning, and eight case scenarios selected from the most common tumor types (head and neck, chest, colorectal, genitourinary, gynecologic and gastrointestinal) reported in the Canadian survey [11]. The completed questionnaires were received via email. Comparisons were made between patients treated in 2004–2009 and those treated in 2010–2014, and between the Canadian survey and the present Japanese survey. This study defined Re-RT as RT performed after previous RT of 30 Gy/10 fractions (= EQD2 36 Gy, using $\alpha/\beta = 3$, where $\text{EQD2} = \text{prescription dose} \times (\alpha/\beta + \text{dose per fraction})/(\alpha/\beta + 2)$, where $\alpha/\beta = 10$ for tumors and 3 for organs at risk.

Statistical analysis

All statistical analyses were performed using Stat-view 5.0 statistical software (SAS Institute, Inc., Cary, NC, USA). The percentage values were analyzed using the $\chi^2$ test, and values were compared using Mann–Whitney U analysis. All analyses used the $P < 0.05$ level of significance.

RESULTS

A total of 34 ROs from 28 institutions returned the survey. All 28 institutions experienced Re-RT cases in 2014. However 26 institutions (93%) had difficulty in obtaining individual Re-RT case details from their respective databases, primarily because there were no accompanying details, such as ‘second RT course’ or ‘in-field cancer recurrence after initial RT’. Only 19 institutions provided detailed information for Re-RT cases (Table 1). Of these, 193 Re-RT cases (institution median = 6; 1–51) occurred in 2014 (Table 1). The most common Re-RT sites were the brain ($n = 55$, 28.9%), vertebral body ($n = 30$, 15.8%), chest ($n = 30$, 15.8%), and head or neck ($n = 28$, 14.7%) in 2014. These figures showed a similar distribution in 2005–2009 (brain = 18%, vertebral body = 19.7%, chest = 24%, head and neck = 15.3%) and in 2010–2014 (brain = 30%, vertebral body = 17.4%, chest = 18.3%, head and neck = 15.3%) except those for the brain ($P = 0.037$; Table 1). The number of Re-RT cases increased from 183 in 2005–2009 (institution median = 4; 2–129) to 562 in 2010–2014 (institution median = 26; 2–225). It should be noted that one new institution was included in 2010–2014 as it received sophisticated equipment after 2010.

Table 1. Patient numbers treated by reirradiation in responding institutes

<table>
<thead>
<tr>
<th></th>
<th>2004–2009 (%)</th>
<th>2010–2014 (%)</th>
<th>P-value</th>
<th>2014 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number</td>
<td>183</td>
<td>562</td>
<td>0.037</td>
<td>193</td>
</tr>
<tr>
<td>Brain</td>
<td>33 (18%)</td>
<td>171 (30%)</td>
<td></td>
<td>55 (28%)</td>
</tr>
<tr>
<td>Head and neck</td>
<td>36 (20%)</td>
<td>86 (15%)</td>
<td></td>
<td>28 (15%)</td>
</tr>
<tr>
<td>Chest</td>
<td>44 (24%)</td>
<td>103 (18%)</td>
<td></td>
<td>30 (16%)</td>
</tr>
<tr>
<td>Abdomen</td>
<td>17 (9%)</td>
<td>41 (7%)</td>
<td></td>
<td>10 (5%)</td>
</tr>
<tr>
<td>Pelvis</td>
<td>9 (5%)</td>
<td>23 (4%)</td>
<td></td>
<td>19 (10%)</td>
</tr>
<tr>
<td>Bone mets</td>
<td>6 (3%)</td>
<td>25 (4%)</td>
<td></td>
<td>12 (6%)</td>
</tr>
<tr>
<td>Vertebrae mets</td>
<td>36 (20%)</td>
<td>98 (17%)</td>
<td></td>
<td>30 (16%)</td>
</tr>
<tr>
<td>Other</td>
<td>2 (1%)</td>
<td>15 (3%)</td>
<td></td>
<td>9 (5%)</td>
</tr>
</tbody>
</table>

Table 2. Demographic data for radiation oncologists (ROs)

<table>
<thead>
<tr>
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<th></th>
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<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;5 years</td>
<td>7</td>
<td>(21%)</td>
<td>35</td>
<td>(19%)</td>
<td>n.s.</td>
</tr>
<tr>
<td>5–10 years</td>
<td>8</td>
<td>(24%)</td>
<td>42</td>
<td>(23%)</td>
<td></td>
</tr>
<tr>
<td>11–20 years</td>
<td>11</td>
<td>(32%)</td>
<td>69</td>
<td>(38%)</td>
<td></td>
</tr>
<tr>
<td>&gt;20 years</td>
<td>8</td>
<td>(24%)</td>
<td>38</td>
<td>(21%)</td>
<td></td>
</tr>
</tbody>
</table>
Respondent demographics and Re-RT eligibility and exclusion criteria
Of the total respondents, 24% had been in practice for > 20 years, whereas 21% had been in practice for < 5 years; these respondent demographics resembled those of the Canadian survey (Table 2) [11]. Respondents were asked to comment on patient factors that would influence their decision to recommend Re-RT. Important factors included age (65%), performance status (PS) (83%), life

Table 3. Factors affecting indication of reirradiation

<table>
<thead>
<tr>
<th>Factor</th>
<th>No. of ROs (%)</th>
<th>No. of Canadian ROs (%)</th>
<th>P-value</th>
<th>Detailed factor</th>
<th>Additional comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>No 12 (35%)</td>
<td>133 (73%)</td>
<td>&lt;0.0001</td>
<td>ECOG 1≥</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Yes 22 (65%)</td>
<td>35 (19%)</td>
<td></td>
<td>ECOG 2≥</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Unc. 0 (0%)</td>
<td>15 (8%)</td>
<td></td>
<td>ECOG 3≥</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>ECOG 4≥</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Unc.</td>
<td></td>
</tr>
<tr>
<td>Performance status</td>
<td>Yes 25 (83%)</td>
<td>128 (70%)</td>
<td>n.s.</td>
<td>1–3 months</td>
<td></td>
</tr>
<tr>
<td></td>
<td>No 6 (20%)</td>
<td>39 (21%)</td>
<td></td>
<td>3–6 months</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Unc. 0 (0%)</td>
<td>16 (9%)</td>
<td></td>
<td>6–12 months</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>≥2 years</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Unc.</td>
<td></td>
</tr>
<tr>
<td>Life expectancy</td>
<td>Yes 21 (70%)</td>
<td>109 (60%)</td>
<td>n.s.</td>
<td>1–3 months</td>
<td></td>
</tr>
<tr>
<td></td>
<td>No 9 (30%)</td>
<td>59 (32%)</td>
<td></td>
<td>3–6 months</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Unc. 1 (4%)</td>
<td>15 (8%)</td>
<td></td>
<td>6–12 months</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>≥2 years</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Unc.</td>
<td></td>
</tr>
<tr>
<td>Distant metastasis</td>
<td>Yes 22 (67%)</td>
<td>99 (54%)</td>
<td>n.s.</td>
<td>1–3 months</td>
<td></td>
</tr>
<tr>
<td></td>
<td>No 11 (33%)</td>
<td>60 (33%)</td>
<td></td>
<td>3–6 months</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Unc. 0 (0%)</td>
<td>23 (13%)</td>
<td></td>
<td>6–12 months</td>
<td></td>
</tr>
<tr>
<td>Disease-free interval after initial RT</td>
<td>Yes 22 (73%)</td>
<td>144 (79%)</td>
<td>n.s.</td>
<td>1–3 months</td>
<td></td>
</tr>
<tr>
<td></td>
<td>No 8 (27%)</td>
<td>25 (14%)</td>
<td></td>
<td>3–6 months</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Unc. 1 (4%)</td>
<td>14 (8%)</td>
<td></td>
<td>6–12 months</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1–2 years</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>≥2 years</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Unc.</td>
<td></td>
</tr>
</tbody>
</table>

Summation of % does not equal 100% because of duplicated answers. ‘Other’ included distance from OAR, patient will. Unc. = uncertain, RO = radiation oncologist, ECOG = Eastern Cooperative Oncology Group.

*One RO replied: ECOG 2≥ for curative Re-RT, ECOG 4≥ for palliation.

†One RO replied: It is case sensitive.

‡One RO replied: >2 months for palliative and >6 months for curative Re-RT.

§Six ROs replied: Yes for curative Re-RT.
expectancy (70%), absence of distant metastases (67%), and interval since initial treatment (73%; Tables 2 and 3). Most respondents believed that patients should have a minimum Eastern Cooperative Oncology Group (ECOG) PS of 2–3, a minimum life expectancy of 6–12 months, and an interval of 6 months or more from initial treatment to be considered for Re-RT (Table 3). These figures were similar to those in the Canadian survey, except those for age, detailed ECOG PS, and time interval since initial therapy. The Canadian survey reported that age did not influence the likelihood of an RO prescribing Re-RT (Table 3) [11].

Factors affecting Re-RT treatment planning
Most ROs suggested that factors such as metastatic work-up (69%), previous total radiation dose (91%) and the BED (68%) were significant considerations when deciding the amount of residual normal tissue tolerance, the Re-RT dose and Re-RT feasibility (Table 4). Significant factors in deciding Re-RT dose were previous dose (74%), clinical judgment (79%) and BED (79%). Only 16% of ROs simultaneously used chemotherapy and Re-RT. Similar respondent attitudes were observed in the present survey and the Canadian survey.

Responses for site-specific case scenarios
Responses to the site-specific questions are summarized in Table 5. In this study, 94% of ROs recommended Re-RT for central nervous system cases, as compared with 34% of ROs in the Canadian survey. Most ROs (18/24 = 75%) recommended SRT, and one recommended stereotactic radiosurgery (SRS) after debulking surgery. In general, > 60% of ROs recommended Re-RT for every scenario, which seems to be higher than the percentage observed in the Canadian survey (34.8–78.8%); however, the opposite trend was observed for cervical cancer recurrence cases (Table 5). Ninety-six percent of Canadian ROs recommended Re-RT in recurrent cervical cancer scenarios, as compared with 82% of Japanese ROs. Japanese ROs recommended only brachytherapy, whereas Canadian ROs recommended external beam radiotherapy (EBRT) + BT.

DISCUSSION
The aim of this study was to survey the present state of Re-RT; this included comparing the attitude towards Re-RT between Japanese ROs in 2015 and Canadian ROs in 2008. The widely prevailing notion that Re-RT cannot be used after a radical course of RT continues to hinder the active management and treatment of patients with in-field cancer recurrence. Factors determining the safe and effective use of Re-RT include primary tumor site, the initial cancer stage, type of initial treatment (radiation dose, technique, dose per fraction, use of concurrent chemotherapy), response to initial treatments, clinically apparent late effects from initial RT, residual radiation tolerance of the normal tissues (including BED calculation), the duration of the relapse-free interval, and the existing literature. Re-RT purpose (radical or palliative) is also an important

<table>
<thead>
<tr>
<th>Table 4. Factors affecting reirradiation planning</th>
<th>No. of ROs</th>
<th>(%)</th>
<th>(%) of Canadian ROs [11]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metastatic work-up Yes</td>
<td>22</td>
<td>(69%)</td>
<td>(72%)</td>
</tr>
<tr>
<td>Metastatic work-up No</td>
<td>4</td>
<td>(13%)</td>
<td></td>
</tr>
<tr>
<td>Metastatic work-up Unc.</td>
<td>6</td>
<td>(19%)</td>
<td></td>
</tr>
<tr>
<td>Normal tissue tolerancea Previous dose</td>
<td>31</td>
<td>(91%)</td>
<td>(90%)</td>
</tr>
<tr>
<td>Normal tissue tolerancea Clinical decision</td>
<td>21</td>
<td>(62%)</td>
<td></td>
</tr>
<tr>
<td>Normal tissue tolerancea BED</td>
<td>23</td>
<td>(68%)</td>
<td>(69%)</td>
</tr>
<tr>
<td>Normal tissue tolerancea Irradiated volume</td>
<td>13</td>
<td>(38%)</td>
<td>(90%)</td>
</tr>
<tr>
<td>Factor to decide Re-RT dosea Previous dose</td>
<td>25</td>
<td>(74%)</td>
<td></td>
</tr>
<tr>
<td>Factor to decide Re-RT dosea Clinical decision</td>
<td>27</td>
<td>(79%)</td>
<td>(83%)</td>
</tr>
<tr>
<td>Factor to decide Re-RT dosea BED</td>
<td>27</td>
<td>(79%)</td>
<td>(53%)</td>
</tr>
<tr>
<td>Factor to decide Re-RT dosea Irradiated volume</td>
<td>13</td>
<td>(38%)</td>
<td></td>
</tr>
<tr>
<td>Factor to decide Re-RT dosea Otherb</td>
<td>1</td>
<td>(3%)</td>
<td></td>
</tr>
<tr>
<td>Chemotherapy use Yes</td>
<td>5</td>
<td>(16%)</td>
<td>(28%)</td>
</tr>
<tr>
<td>Chemotherapy use No</td>
<td>16</td>
<td>(50%)</td>
<td></td>
</tr>
<tr>
<td>Chemotherapy use Unc.</td>
<td>11</td>
<td>(34%)</td>
<td></td>
</tr>
</tbody>
</table>

*aSummation of % does not equal 100% because of duplicated answers.

*bOther’ included distance from organs at risk, patient will. Unc. = uncertain, RO = radiation oncologist.
Table 5. Attitude to reirradiation for site-specific case scenarios

<table>
<thead>
<tr>
<th>Case No.</th>
<th>RO’s answer (%) of Canadian ROs [11]</th>
<th>Initial indication (in descending order)</th>
<th>Reason for Re-RT decision (in descending order)</th>
<th>Methods and dose fractionation (in descending order)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes No Unc. (% ‘Yes’ ‘Yes’ ‘Yes’)</td>
<td></td>
<td></td>
<td>RO’s answer Canadian ROs [11]</td>
</tr>
<tr>
<td>1</td>
<td>Central nervous system</td>
<td>Curative</td>
<td>Yes (No other option left) (For QOL maintenance)</td>
<td>SRT (25–48 Gy/3–8 fr), IMRT (20–40 Gy/7–15 fr), SRS, BT (25–30 Gy/5–10 fr)</td>
</tr>
<tr>
<td></td>
<td>30 2 0 (94%) (34.8%)</td>
<td>(Modern technology: SRT and IMRT available)</td>
<td>(Young age) No (Risk of brain necrosis) (Surgery preferred)</td>
<td>SRS (15 Gy or 18 Gy/1 fr), 3D-CRT EBRT (20 Gy/10 fr, 25–40 Gy/20 fr, 30 Gy/5 fr²)</td>
</tr>
<tr>
<td>2</td>
<td>Head and neck ca. (nasopharyngeal cancer)</td>
<td>Curative</td>
<td>Yes (No other option left) (More effective than chemotherapy)</td>
<td>IMRT (40–70 Gy/20–35 fr), SBRT (20–40 Gy/5–10 fr), 3D-CRT, BT (18–48 Gy/6–12 fr bid)</td>
</tr>
<tr>
<td></td>
<td>27 4 0 (87%) (78.8%)</td>
<td>No (Surgery preferred) (Chemotherapy preferred)</td>
<td>(Risk of visual disturbance)</td>
<td>3D-CRT, IMRT, SRS (18 Gy/1 fr), BT,EBRT (50–70 Gy/25–35 fr, 60 Gy/25 fr, 50 Gy/20 fr, bid 50 or 60 Gy/40 fr/4 weeks)</td>
</tr>
<tr>
<td>3</td>
<td>Non–small cell lung ca.</td>
<td>Curative</td>
<td>Yes (Useful for palliation more than CTX) (QOL maintenance; hemesputum prophylaxis) (Yes for peripheral lesion, but no for central lesion) (SBRT, IMRT, Particle radiotherapy preferred)</td>
<td>3D-CRT (30–50 Gy/10–25 fr), IMRT (30 Gy/10 fr, 48–60 Gy/20 fr, 50–56 Gy/25–33 fr), SBRT (40–60 Gy/4–10 fr, 25 Gy/5 fr)</td>
</tr>
<tr>
<td></td>
<td>23 7 2 (72%) (65%)</td>
<td>(Long interval) No (Depend on place and recurrent pattern) (Primary and lymph node area could be too large to Re-RT) (Difficult to identify the lesion from radiation fibrosis) Unc. (Yes for peripheral tumor, but no for central tumor)</td>
<td></td>
<td>3D-CRT, conventional RT, endobronchial BT (8 Gy/1 fr, 14–15 Gy/2–3 fr/2–3 weeks), IMRT EBRT (30 Gy/10–15 fr, 36 Gy/12 fr, 25 Gy/10 fr, 20 Gy/5 fr)</td>
</tr>
<tr>
<td>4</td>
<td>Breast ca.</td>
<td>Curative</td>
<td>Yes (Long interval from initial RT) (Curative potential for oligo recurrence) (Skin could tolerable) (No serious OAR involved except skin) (There was a reference for this case)</td>
<td>3D-CRT (40–60 Gy/20–30 fr), Electron (50–60 Gy/25–30 fr), IMRT (40–56 Gy/20–33 fr)</td>
</tr>
<tr>
<td></td>
<td>21 11 0 (66%) (51.9%)</td>
<td></td>
<td></td>
<td>Electron therapy, 2D RT, BT (50 Gy LDR or 20–25 Gy HDR/4–5 fr bid/2–2.5 days), 3D-CRT, IMRT EBRT (30–50 Gy/15–25 r, 30–50 Gy/30 fr bid/2 weeks)</td>
</tr>
<tr>
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<td></td>
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<td>Continued</td>
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Questionnaire survey for Re-RT
<table>
<thead>
<tr>
<th>Case No.</th>
<th>Initial indication</th>
<th>Reason for Re-RT decision</th>
<th>Methods and dose fractionation (in descending order)</th>
<th>RO's answer</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Brain metastasis (breast)</strong></td>
<td>Palliative</td>
<td>(No other option left) (Small lesion) (Palliative merit) (According to patient’s will) (Brain could be tolerated up to 60 Gy)</td>
<td>SBRT (18–25 Gy/1 fr, 30–36 Gy/3 fr), 3D-CRT (30–40 Gy/5–10 fr), IMRT (45–60 Gy/15 fr, 35 Gy/5 fr)</td>
<td>Not available</td>
</tr>
<tr>
<td>5</td>
<td>Not available</td>
<td>No (Hormonal Tx preferred) (Prophylaxis Re-RT may be overtreatment) (No symptom) (Retained to recurrence) (Toxicity concern)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Cervical ca.</strong></td>
<td>Curative</td>
<td>(No other option left) (Curative possibility) (Brachytherapy could avoid severe toxicity)</td>
<td>BT (HDR 18–25 Gy/4–5 fr, 36–42 Gy/6–5 fr), SBRT and IMRT (20 Gy/5 fr – 48 Gy/8 fr)</td>
<td>3D-CRT, IMRT, 2D EBRT followed by BT (40–50 Gy/20–25 fr/4–5 weeks) followed by BT (LDR) 60–65 Gy EBRT alone (45 Gy/25 fr, 40 Gy/20 fr, 30 Gy/20 fr) BT alone (35–50 Gy LDR/4–6 days or 20–25 Gy HDR/4–5 fr bid/2–2.5 days)</td>
</tr>
<tr>
<td>6</td>
<td></td>
<td>No (Surgery preferred) (Toxicity concern)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Rectal ca.</strong></td>
<td>Curative</td>
<td>(No other option left) (Particle therapy preferred) (Palliative merit: pain relief) (BT possible)</td>
<td>IMRT (30–40 Gy/50 fr, 50–66 Gy/20–25 fr, 30 Gy/10 fr), 3D-CRT (30 Gy/10 fr, 20 Gy/5 fr, 8 Gy/1 fr, 40 Gy/20 fr), Charged particle, BT (8 Gy/1 fr, 20–30 Gy, 66 Gy/33 fr; SIB)</td>
<td>3D-CRT, conventional RT, SRS, IMRT EBRT (30 Gy/10 fr, 20 Gy/5 fr, 20 Gy/10 fr, 5–8 Gy/1 fr)</td>
</tr>
<tr>
<td>7</td>
<td></td>
<td>No (Re-RT is not routine protocol) (Toxicity concern)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
determinant, which is influenced by the presence of distant metastases (other active lesions), PS and age. Although age and PS were important factors in Japan, the Canadian survey showed that there were not limiting factors when deciding whether Re-RT was needed (Tables 1, 2), possibly reflecting the attitudes changing from palliative to curative intentions with current challenges with using advanced technology today [11].

Re-RT cases increased in number from 2005–2009 to 2010–2014, indicating that ROs are becoming more familiar with Re-RT; this was also true in the comparison between the present survey and the Canadian survey [11]. This may have been because RT technology has considerably improved during this decade, and more patients are receiving Re-RT therapy using state-of-the-art equipment. Re-RT has been successfully used with acceptable morbidity for a variety of locally recurrent tumors, including tumors of the breast, head and neck, brain, pelvis, bone and lung [6]. However, occasionally lethal side effects such as carotid blow-out syndrome may occur [12]. The risks of normal tissue complications and the lack of adequate data on recovery from radiation injury were the common barriers to using Re-RT as a salvage treatment modality. Acutely responding tissues fully recover within a few months, and these tissues can tolerate retreatment as well as untreated tissue [13]. On the other hand, the pattern of recovery from radiation injury varied considerably in late-responding tissues. Late-responding tissues (the heart, bladder and kidney) do not exhibit long-term recovery, whereas the skin, mucosa, lung, and spinal cord do recover from occult injury of varying magnitudes [9]. Several studies have analyzed the suitability of Re-RT for in-field cancer recurrence and reported that Re-RT (with or without chemotherapy) results in adequate loco-regional tumor and symptom control [5–7, 14–17].

An additional barrier to the use of Re-RT is the paucity of data available to determine the Re-RT schedule and dose fractionation–volume relationships, although hyperfractionated schedules or day-after-day schedules were suggested as a means of limiting retreatment toxicity [18, 19]. In addition, newly installed technology (SRT, IMRT, IGRT, particle therapy and image-guided brachytherapy) increased the Re-RT potential, which simultaneously made it more difficult to establish a clear consensus on Re-RT. For example, charged particle therapy was recommended for several recurrence sites in this survey (Table 5); this was not observed in the Canadian survey [11]. Recently, newer technologies, such as 3D conformal radiotherapy (3D-CRT), IMRT, SRS, SRT and charged particle therapy, have influenced Re-RT planning and delivery to facilitate normal tissue tolerance. For example, in this survey three ROs recommended charged particle radiotherapy for rectal cancer.

The consensus on palliative or curative intention has also been changing recently; the oligometastasis concept illustrates this [20]. Furthermore, the presently available database systems do not facilitate the easy retrieval of Re-RT cases. Most institutions reported difficulty in retrieving Re-RT case information. Some institutions examined the data for all patients that received RT twice or more, to identify the overlap between initial RT fields and the Re-RT field. An easy system for Re-RT case information retrieval from databases is essential for the future exploration of Re-RT utility. Finally, future studies should also take into account the quality of life for patients who undergo Re-RT.

In conclusion, this decade saw an increase in the number of Re-RT cases and RO interest in Re-RT as a viable therapeutic option.
However, further consensus building is required, to establish guidelines for practice and prospective evaluation.

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CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest.

REFERENCES