




















# Looking Back: International Practice Patterns in Breast Radiation Oncology From a Case-Based Survey Across 54 Countries During the First Surge of the COVID-19 Pandemic

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## ABSTRACT

**PURPOSE** The COVID-19 pandemic has profoundly affected cancer care worldwide, including radiation therapy (RT) for breast cancer (BC), because of risk-based resource allocation. We report the evolution of international breast RT practices during the beginning of the pandemic, focusing on differences in treatment recommendations between countries.

**MATERIALS AND METHODS** Between July and November 2020, a 58-question survey was distributed to radiation oncologists (ROs) through international professional societies. Changes in RT decision making during the first surge of the pandemic were evaluated across six hypothetical scenarios, including the management of ductal carcinoma in situ (DCIS), early-stage, locally advanced, and metastatic BC. The significance of changes in responses before and during the pandemic was examined using chi-square and McNemar-Bowker tests.

**RESULTS** One thousand one hundred three ROs from 54 countries completed the survey. Incomplete responses (254) were excluded from the analysis. Most respondents were from the United States (285), Japan (117), Italy (63), Canada (58), and Brazil (56). Twenty-one percent (230) of respondents reported treating at least one patient with BC who was COVID-19-positive. Approximately 60% of respondents reported no change in treatment recommendation during the pandemic, except for patients with metastatic disease, for which 57.7% (636/1,103;  $P < .0005$ ) changed their palliative practice. Among respondents who noted a change in their recommendation during the first surge of the pandemic, omitting, delaying, and adopting short-course RT were the most frequent changes, with most transitioning to moderate hypofractionation for DCIS and early-stage BC.

**CONCLUSION** Early in the COVID-19 pandemic, significant changes in global RT practice patterns for BC were introduced. The impact of published results from the FAST FORWARD trial supporting ultrahypofractionation likely confounded the interpretation of the pandemic's independent influence on RT delivery.

## ACCOMPANYING CONTENT

 [Data Supplement](#)

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## INTRODUCTION

The COVID-19 pandemic affected radiation therapy (RT) for breast cancer (BC) delivery worldwide. To maximize clinical resources and minimize COVID-19 transmission, radiation oncologists (ROs) modified BC treatments as international professional societies established guidelines.<sup>1-5</sup>

These guidelines reflected patterns encouraging delayed RT for low-risk BC patients<sup>6-9</sup> (less so for advanced-stage BC),<sup>7,10</sup> abbreviating treatment regimens,<sup>6,8,11</sup> and decreasing systemic therapy compared with surgery.<sup>6</sup> Oncologists also reduced patient visitation, recommending initial surgery over preoperative chemotherapy,<sup>6,8</sup> and delayed reconstructive surgery after mastectomy.<sup>8,10</sup>

## CONTEXT

### Key Objective

To examine the international evolution of breast radiation therapy (RT) practices during the early stages of the COVID-19 pandemic and identify differences in treatment recommendations between countries.

### Knowledge Generated

A survey conducted between July and November 2020 involving 1,103 radiation oncologists (ROs) from 54 countries found that approximately 60% of respondents reported no change in their treatment recommendations during the pandemic. The most frequent changes included omitting, delaying, or adopting short-course RT, with many transitioning to moderate hypofractionation.

### Relevance

The pandemic significantly influenced RT delivery for breast cancer, as ROs worldwide swiftly embraced shorter fractionation courses. Alongside the publication of relevant clinical trials during the pandemic and ongoing studies, the trend toward widespread adoption of hypofractionation appears increasingly likely.

While institutions,<sup>12-14</sup> nations,<sup>8,11,15-17</sup> and regions<sup>6,7,10,18,19</sup> reported treatment modifications during COVID-19's peak, the global impact on BC treatment modification has not been collectively assessed. Our unique study is the only case-based global survey evaluating changes to RT recommendations for BC during the pandemic's first surge, which varied by country.

## MATERIALS AND METHODS

The BC radiation oncology team at Massachusetts General Hospital and Dana Farber Cancer Institute (Boston, MA) initiated an international collaboration of ROs in developing a case-based survey evaluating BC RT decision-making changes during the pandemic's surge across six scenarios, meeting regularly through teleconference to develop it.

Consisting of 6 cases and 58 questions (Data Supplement), the survey was approved by Dana Farber/Harvard Cancer Center's institutional review board and was distributed to ROs who self-identified as having treated at least one patient with BC annually, with an international network of radiation oncology professional societies augmenting distribution (Table 1). It contained the following scenarios: (1) low-grade ductal carcinoma in situ (DCIS), (2) low-risk invasive BC after breast-conserving surgery, (3) early-stage invasive BC after mastectomy with immediate reconstruction, (4) invasive BC after neoadjuvant chemotherapy (NAC) and mastectomy without reconstruction, (5) invasive BC after mastectomy without reconstruction and with adjuvant chemotherapy, and (6) metastatic BC with an enlarging and bleeding breast mass. Respondents provided recommendations for two scenarios: (1) pre-pandemic and (2) during the pandemic's surge. Conventional fractionation was defined as 1.8-2.3 Gy per fraction, moderate hypofractionation as 2.31-3.0 Gy, and ultrahypofractionation as >5 Gy.

The survey was translated into Spanish, Russian, and Mandarin, and distributed through REDCap on July 17, 2020, closing on November 8, 2020. Anonymous responses were compiled into a secure central database (incomplete responses were excluded [n = 254]). Categorical variables were described as counts and percentages, with chi-square and McNemar-Bowker tests used to examine the significance of changes between pre-pandemic and surge. P values are reported with statistical significance defined as <0.05. Statistical analysis was performed with R Studio, v. 2021.09.0 + 351 (Posit PBC, Boston, MA), and Excel 365, v. 2021 (Microsoft, Redmond, WA). This study was approved by Partners IRB (Protocol no.: 2020P001416) and nonverbal informed consent was obtained from participants before taking the survey by attesting on the webpage.

## RESULTS

Overall, 1,103 ROs from 54 countries completed the survey (Fig 1), with the most respondents from 13 countries: United States (n = 285), Japan (n = 117), Italy (n = 63), Canada (n = 58), Brazil (n = 56), France (n = 48), Spain (n = 44), Russia (n = 43), China (n = 42), Thailand (n = 38), South Korea (n = 38), United Kingdom (n = 35), and Saudi Arabia (n = 31). ROs practiced in urban (69.8%; n = 770), suburban (19.4%; n = 214), rural (9.6%; n = 106), and other settings (1.2%; n = 13). Additionally, 49.8% (n = 549) practiced in university-affiliated hospitals, 25.7% (n = 283) in private practice, 21.1% (n = 233) in government hospitals, and 3.4% (n = 38) in other centers. Most (74.4%; n = 821) reported treating <200 patients with BC annually, while 45.6% (n = 503) reported >500 patients. In addition, 311 (28.2%) reported ≥1 patient with BC who was COVID-19-positive between November 1, 2019, and July 1, 2020. Herein, we describe treatment recommendation changes during the pandemic's surge as analyzed within six clinical cases.

**TABLE 1.** Participating Radiation Oncology Professional Societies/Group

Country	Professional Society/Group
United States	American Society for Radiation Oncology (ASTRO)
France and China	Sino-French Association of Radiation Oncology Radiation Oncology of the West of China
Japan	Japanese Society for Radiation Oncology
Italy	Italian Association for Radiotherapy and Clinical Oncology (AIRO)
Canada	Canadian Association of Radiation Oncologists (CARO)
Russia	Russian Radiation Oncology Society (ROS)
Spain	Spanish Society of Radiotherapeutic Oncology (SEOR)
South Korea	The Korean Society for Radiation Oncology (KOSRO)
United Kingdom	United Kingdom Breast Cancer Group (UKBCG)
Saudi Arabia	Saudi Assembly for Radiation Oncology (SARO)
South Africa	South African Oncology Consortium (SAOC)
Germany	Deutsche Gesellschaft für Radioonkologie (DEGRO)
Israel	National Radiation Oncology Forum (NROF)
Denmark	Danish Breast Cancer Group RT Committee (DBCg)

## Case 1

### DCIS

A 52-year-old woman was diagnosed with 1.5-cm grade 2 ER+/PR+ DCIS and treated with left lumpectomy with final surgical margins >2 mm. Adjuvant endocrine therapy was initiated (Fig 2A).

Prepandemic, 80.8% of respondents recommended adjuvant whole-breast RT (WBRT), 12.4% (n = 137) partial breast irradiation (PBI), 6.0% (n = 66) RT omission, and 0.8% (n = 9) delayed RT. In comparison, during the pandemic's surge, significantly more recommended delaying (22.3%, n = 246;  $P < .005$ ) or omitting RT (12.9%, n = 142;  $P < .005$ ). ROs from United States (40.7%), Saudi Arabia (25.8%), Canada (25.4%), and Brazil (23.2%) were most likely to delay RT during the surge, while ROs in Russia (39.5%) and Thailand (20.5%) would omit RT. Among those recommending delayed RT, most recommended an 11- to 16-week delay (22.2%, 2/9, prepandemic v 52.8%, 131/248, during surge;  $P < .005$ ), while others a 17- to 24-week delay (11.1%, 1/9, prepandemic v 29.4%, 73/248, during surge;  $P < .005$ ).

Of those recommending WBRT prepandemic (n = 891), 77.1% (n = 687) chose moderate hypofractionation, and 67.9% (n = 605) omitted a lumpectomy site boost. During the surge, significantly more recommended ultrahypofractionation (1.2%, 11/891, prepandemic to 10.5%, 61/581, during the surge;  $P < .005$ ). Changes in fractionation varied widely, with ROs in United Kingdom (90.5%), Canada (38.9%), Spain (32.0%), and Saudi Arabia (16.7%) reporting the highest ultrahypofractionated breast RT rates during the surge. By contrast, ultrahypofractionation

for DCIS was infrequent in China (6.7%), United States (3.8%), and Italy (2.3%). No respondents from Japan, France, Russia, South Korea, or South Africa recommended ultrahypofractionation for DCIS.

The most common PBI modality recommended for DCIS was external-beam RT (72.2%, 99/137), with 31.3% (31/99) favoring 30 Gy in five fractions over 2 weeks (Florence schedule), while 47.5% (47/99) favored >10 fraction regimens. This proportion shifted during the surge, with 31.3% (31/99 prepandemic) versus 58.6% (58/99 during surge;  $P < .005$ ) recommending a five-fraction regimen.

## Case 2

### Early-Stage Invasive BC After Breast-Conserving Surgery

A 61-year-old woman underwent a right lumpectomy revealing a 2-cm grade 2 ER+/PR+/HER2– invasive lobular carcinoma with no evidence of lymphovascular invasion. Out of two sentinel nodes, zero contained malignancy. Her Oncotype Dx recurrence score was 8. Endocrine therapy was initiated (Fig 2B).

Prepandemic, 83% (n = 915) recommended WBRT, 14.7% (n = 162) PBI, 1.6% (n = 18) RT omission, and 0.6% (n = 7) RT delay. A significant increase recommended delayed RT during the surge (19.0%, n = 210;  $P < .005$ ). Respondents in United States, Thailand, Canada, Saudi Arabia, and Japan reported the highest delayed-RT rates (35.0%, 20.5%, 20.3%, 19.4%, and 17.9%, respectively). There was a slight increase in omitting RT across all countries during the surge (4.6%, n = 51;  $P < .005$ ); however, ROs in Russia (18.6%), Saudi Arabia (9.7%), United Kingdom (8.9%), Thailand (7.7%), and Brazil (7.1%) favored omitting RT.

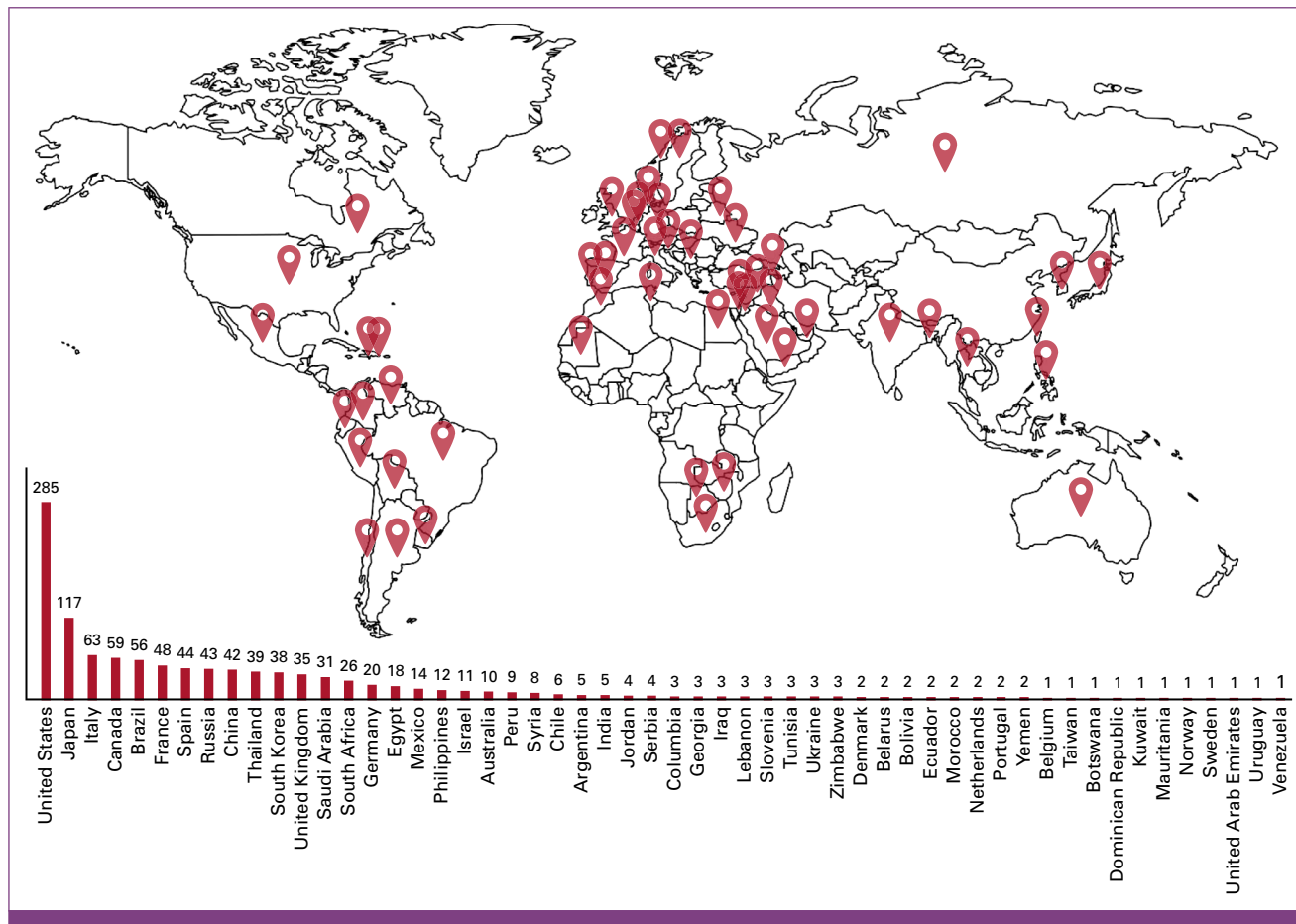


FIG 1. Total responses across 54 participating countries.

Moderate hypofractionation was the most popular WBRT regimen, with a significant change between pre-pandemic and surge (80.8%, 739/915, and 69.4%, 459/661;  $P < .005$ , respectively); during the surge, there was a significant increase in ultrahypofractionation (2.6%, 24/915, pre-pandemic  $v$  16.5%, 109/661, during surge;  $P < .005$ ). Respondents in United Kingdom (89.3%), Spain (58.6%), Canada (51.5%), and Saudi Arabia (45.0%) recommended ultrahypofractionated WBRT during the surge, while those in South Africa (11.1%), Italy (10.8%), China (5.9%), United States (3.8%), and South Korea (3.4%) infrequently recommended it (no respondents in Japan, France, or Russia recommended it). For those recommending PBI, there was an increase in  $\leq 5$  fractions during the surge compared with pre-pandemic (61.3%, 84/137,  $v$  36.8%, 43/117, respectively;  $P < .005$ ).

### Case 3

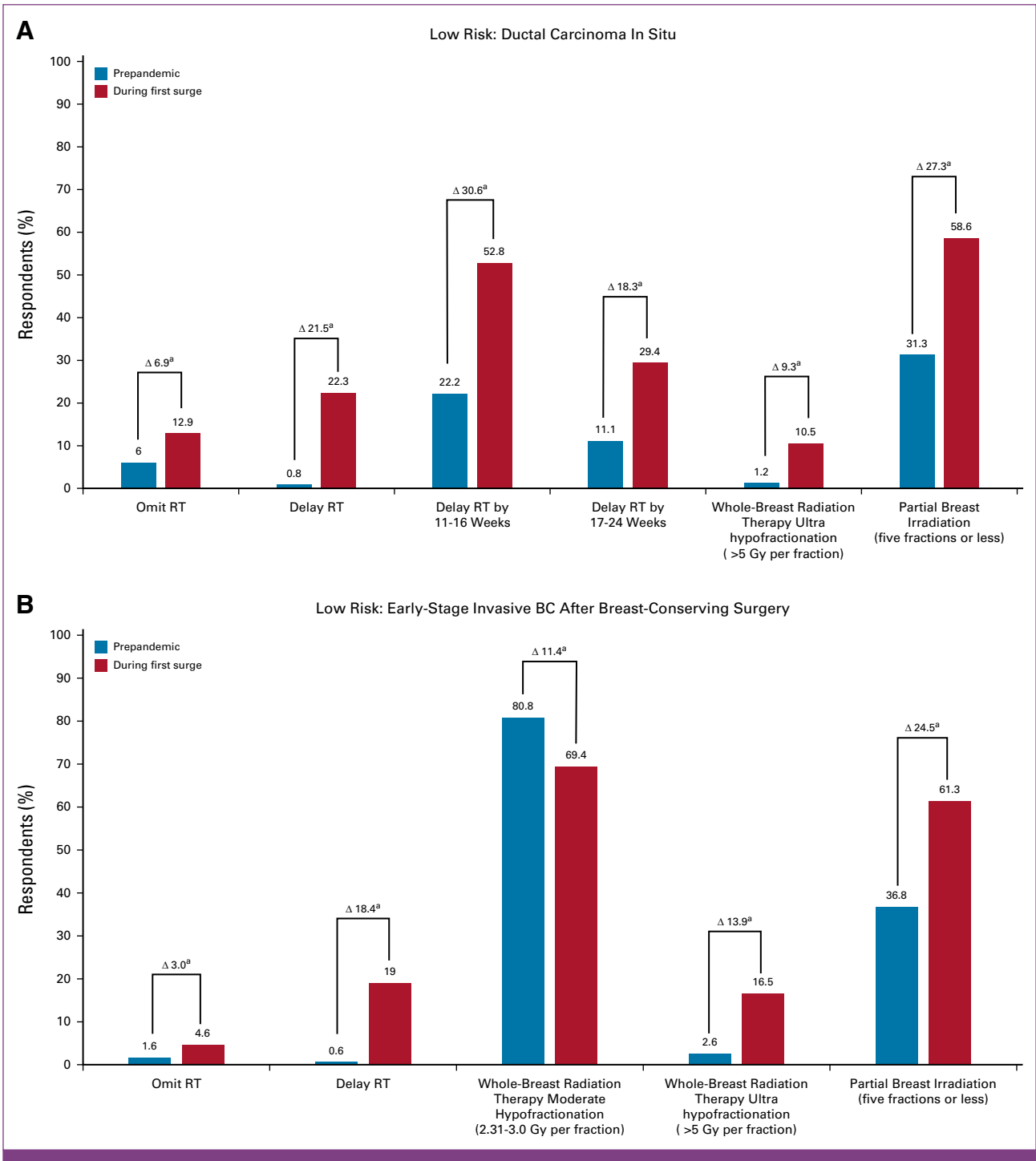
#### *Invasive BC After Mastectomy With Immediate Reconstruction*

A 54-year-old woman underwent a total simple mastectomy with immediate tissue expander reconstruction revealing a 3.4-cm grade 2 ER+/PR+/HER2- invasive ductal carcinoma and no lymphovascular invasion. Of three sentinel lymph nodes, one was positive (8-mm focus) without extranodal

extension. The Oncotype Dx recurrence score was 4. Adjuvant chemotherapy was not recommended. An adjuvant aromatase inhibitor was planned (Fig 3).

Pre-pandemic, most (69.0%, 761) recommended postmastectomy RT (PMRT), whereas a minority favored complete axillary dissection (18.1%, 200) or no further local-regional treatment (12.9%;  $n = 142$ ). ROs in Spain (81.8%), Canada (81.4%), Brazil (80.4%), Thailand (79.5%), and South Korea (78.9%) favored PMRT, while those in Italy (44.4%) and Russia (41.9%) favored complete axillary dissection. During the surge, there was an increase in no further local-regional treatment (20.8%,  $n = 229$ ;  $P < .005$ ). However, PMRT (63.0%,  $n = 695$ ;  $P < .005$ ) and complete axillary dissection (16.2%,  $n = 179$ ;  $P = .106$ ) recommendations decreased, but only the former was statistically significant. ROs in Japan (35.0%), Italy (33.3%), Russia (32.5%), and China (31.0%) most recommended no further local-regional treatment.

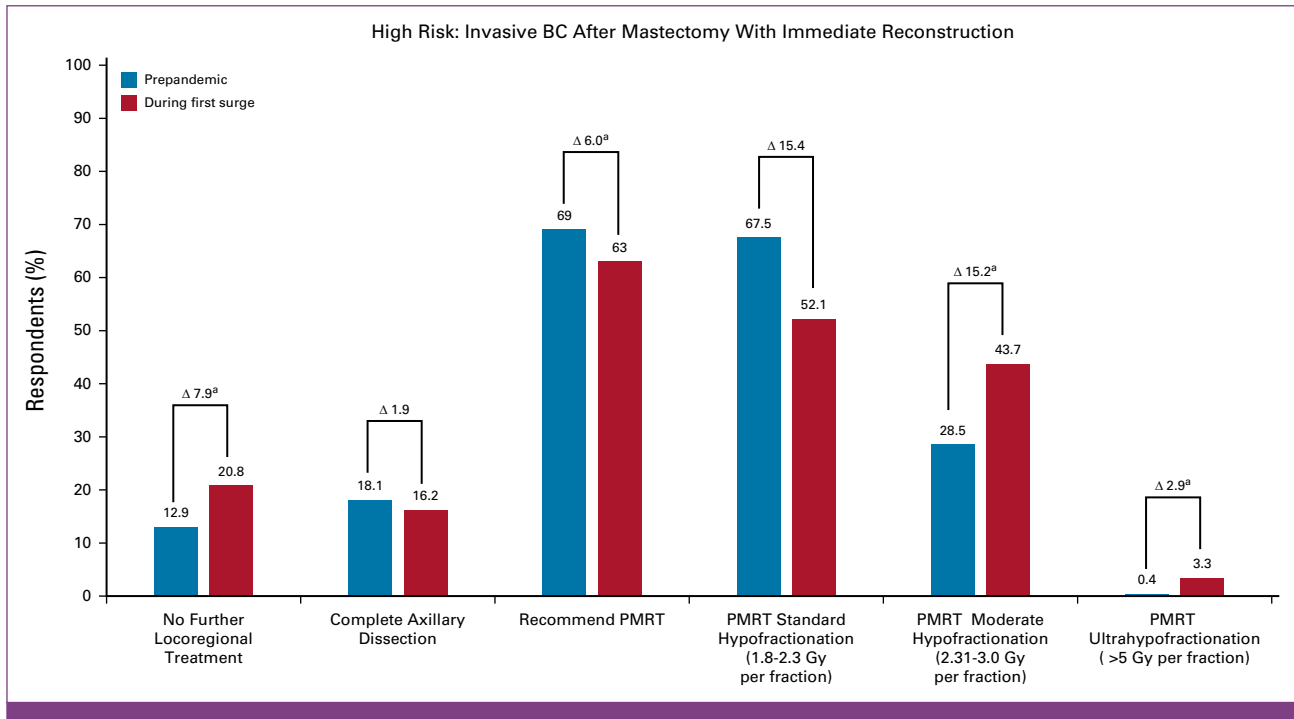
Most ROs recommending PMRT chose conventional fractionation, regardless of pre-pandemic or surge (67.5%, 534/791, and 52.1%, 362/695, respectively). However, during the surge, recommendations significantly increased for moderate hypofractionation (from 28.5%, 217/761, to 43.7%, 304/695;  $P < .005$ ) and ultrahypofractionation (from 0.4%,



**FIG 2.** (A) Distribution of responses on treatment guidelines followed before and during the COVID surge among 1,103 respondents regarding a DCIS case 1. A 52-year-old woman was diagnosed with 1.5-cm grade 2, ER+/PR+ DCIS and treated with a left lumpectomy with final surgical margins >2 mm. Adjuvant endocrine therapy was initiated. (B) Distribution of responses on treatment guidelines followed before and during the COVID surge among 1,103 respondents regarding an early-stage invasive BC after breast-conserving surgery case 2. A 61-year-old female underwent a right lumpectomy revealing a 2-cm grade 2, ER+, PR+, HER2– invasive lobular carcinoma with no evidence of lymphovascular invasion. Neither of two sentinel nodes contained malignancy. The Oncotype Dx recurrence score was 8. Endocrine therapy was initiated. <sup>a</sup>Responses regarding treatment recommendation are shown. BC, breast cancer; DCIS, ductal carcinoma in situ; ER+, estrogen receptor–positive; HER2–, human epidermal growth factor receptor 2–negative; PR+, progesterone receptor–positive; RT, radiation therapy.

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**FIG 3.** Distribution of responses on treatment guidelines followed before and during the COVID surge among 1,103 respondents regarding an invasive BC after mastectomy with immediate reconstruction case 3. A 54-year-old woman underwent a total simple mastectomy with immediate tissue expander reconstruction. Pathology revealed a 3.4-cm grade 2 ER+/PR+/HER2- invasive ductal carcinoma and no lymphovascular invasion. Of three sentinel lymph nodes, one was positive (8-mm focus) without extranodal extension. Oncotype Dx recurrence score was 4. Adjuvant chemotherapy was not recommended. An adjuvant aromatase inhibitor was planned. ªResponses regarding treatment recommendation are shown. BC, breast cancer; ER+, estrogen receptor-positive; HER2-, human epidermal growth factor receptor 2-negative; PMRT, postmastectomy radiation therapy; PR+, progesterone receptor-positive.

3/761, to 3.3%, 23/695;  $P < .005$ ). ROs in Canada, Spain, Brazil, United Kingdom, and Saudi Arabia most recommended moderate hypofractionation prepandemic (39.6%, 55.6%, 46.7%, 87.0%, and 60.9%, respectively) and during surge (70.8%, 66.7%, 63.6%, 63.6%, and 57.1%, respectively). Overall, ROs in United Kingdom (36.4%), Spain (12.1%), and Saudi Arabia (48.0%) had the highest rate of recommending an ultrahypofractionation regimen for PMRT during the surge.

#### Case 4

##### *Invasive BC After NAC and Mastectomy*

A 55-year-old woman with cT2N1 grade 3 triple-negative BC underwent NAC with doxorubicin, cyclophosphamide, and paclitaxel, followed by total mastectomy and sentinel lymph node biopsy. Reconstruction was not performed. A pathologic complete response was achieved, with no residual disease seen in the breast and three sentinel nodes (ypT0N0; Fig 4).

Prepandemic, most recommended PMRT using conventional fractionation (62.3%,  $n = 687$ ) compared with moderate hypofractionation (27.9%,  $n = 308$ ), 3.1–5.0 Gy (0.7%, 8), ultrahypofractionation (0.6%,  $n = 7$ ), or no PMRT (8.4%, 93). However, during the surge, moderate

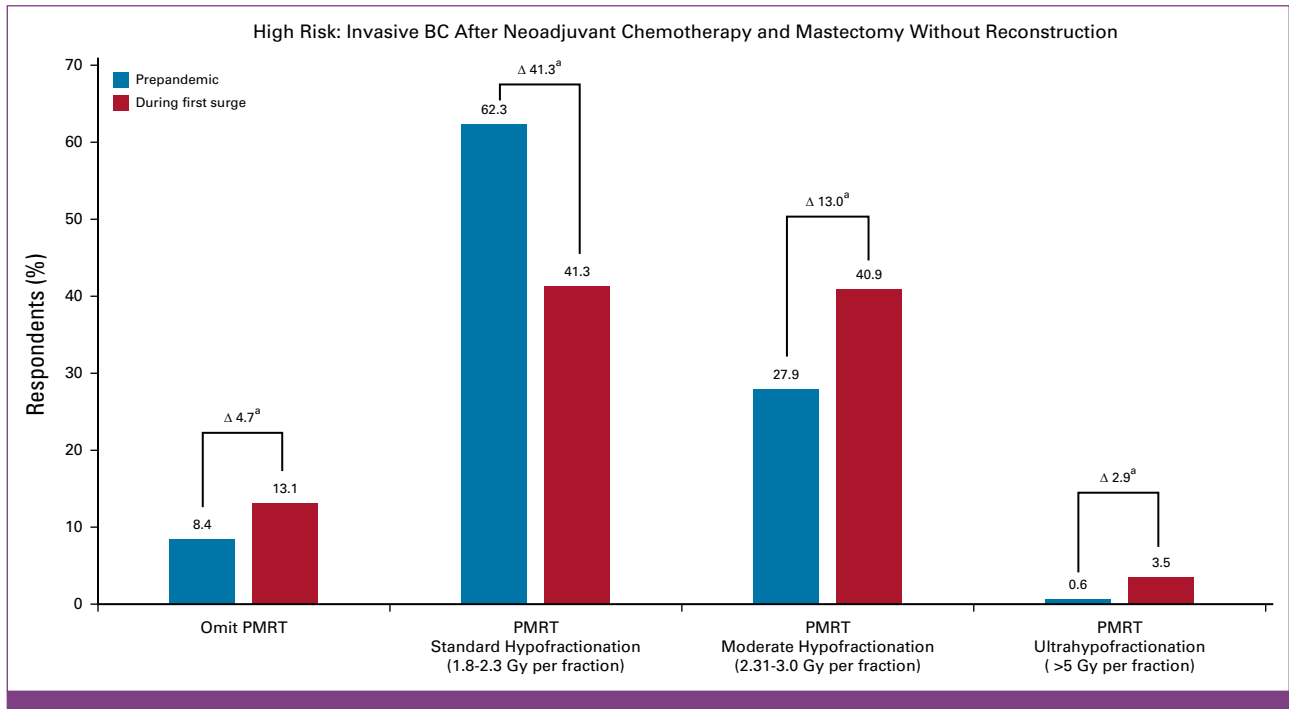
hypofractionation (40.9%,  $n = 451$ ;  $P < .005$ ), no PMRT (13.1%,  $n = 144$ ;  $P < .005$ ), and ultrahypofractionated PMRT (3.5%,  $n = 39$ ;  $P < .005$ ) were recommended. During the surge, respondents from Canada (86.5%), Saudi Arabia (77.8%), Spain (77.5%), Brazil (69.8%), and Russia (63.6%) mostly recommended moderate hypofractionation, while those in China (23.4%), Japan (21.9%), and Saudi Arabia (14.8%) mostly omitted PMRT. In this scenario, ROs in United Kingdom reported the highest ultrahypofractionation use (66.7%).

#### Case 5

##### *Invasive BC After Mastectomy Without Reconstruction and Adjuvant Chemotherapy*

A 45-year-old woman underwent a left modified radical mastectomy without immediate reconstruction. Pathology revealed a 5-cm, grade 2 ER+/PR+/HER- invasive ductal carcinoma with evidence of lymphovascular invasion and five out of 15 positive axillary nodes. She completed adjuvant dose-dense doxorubicin, cyclophosphamide, and paclitaxel. An aromatase inhibitor was planned (Fig 5A).

Prepandemic, most ROs (81.6%, 900) preferred to begin PMRT  $\leq 6$  weeks after surgery, while 16.5% ( $n = 182$ ) would



**FIG 4.** Distribution of responses on treatment guidelines followed before and during the COVID surge among 1,103 respondents regarding an invasive BC after NAC and mastectomy without reconstruction case 4. A 55-year-old woman with cT2N1, grade 3 triple-negative BC underwent NAC with doxorubicin, cyclophosphamide, and paclitaxel, followed by a total mastectomy and sentinel lymph node biopsy. Reconstruction was not performed. A pathologic complete response was achieved with no residual disease seen in the breast and three sentinel nodes (ypT0N0). <sup>a</sup>Responses regarding treatment recommendation are shown. BC, breast cancer; NAC, neoadjuvant chemotherapy; PMRT, postmastectomy radiation therapy.

initiate PMRT >6–10 weeks after surgery. During the surge, recommendations increased for PMRT to start within 6–10 weeks after surgery (23.5%, n = 259; P < .005) or delay by 11–16 weeks after (5.2%, n = 57; P < .005). Most did not change their recommendation to delay RT during the surge, preferring to start <6 weeks (70.2%, n = 774). The surge did not change bolus or boost fractionation or use. Most recommended conventional fractionation (73.3%, n = 808 and 69.0%, n = 761), using a bolus (55.1%, n = 608, and 53.5%, n = 590), and preferring not to boost the mastectomy scar (75.6%, n = 834, and 78.2%, n = 863). Recommended target volume(s) included the chest wall, axillary nodes, and supraclavicular nodes (46.5%, n = 512), with 52.6% (n = 580) also including the internal mammary nodes, which remained relatively consistent during the surge (49.3%, n = 543, and 49.6%, n = 547, respectively). When the same hypothetical patient underwent immediate breast reconstruction with an implant or tissue expander, most recommended conventional fractionation (81.7%, n = 901, and 69.0%, n = 761) compared with moderate hypofractionation (17.3%, n = 191, and 28.9%, n = 319), prepandemic and surge, respectively.

**Case 6**

*Metastatic BC With an Enlarging Breast Mass*

A 75-year-old woman with metastatic ER+/PR+/HER2–invasive ductal carcinoma resistant to several lines of systemic therapy presents with an enlarging and bleeding 6-cm

right breast mass. Karnofsky performance status is 80. Surgical resection is not planned because of the presence of multiple lung metastases (Fig 6).

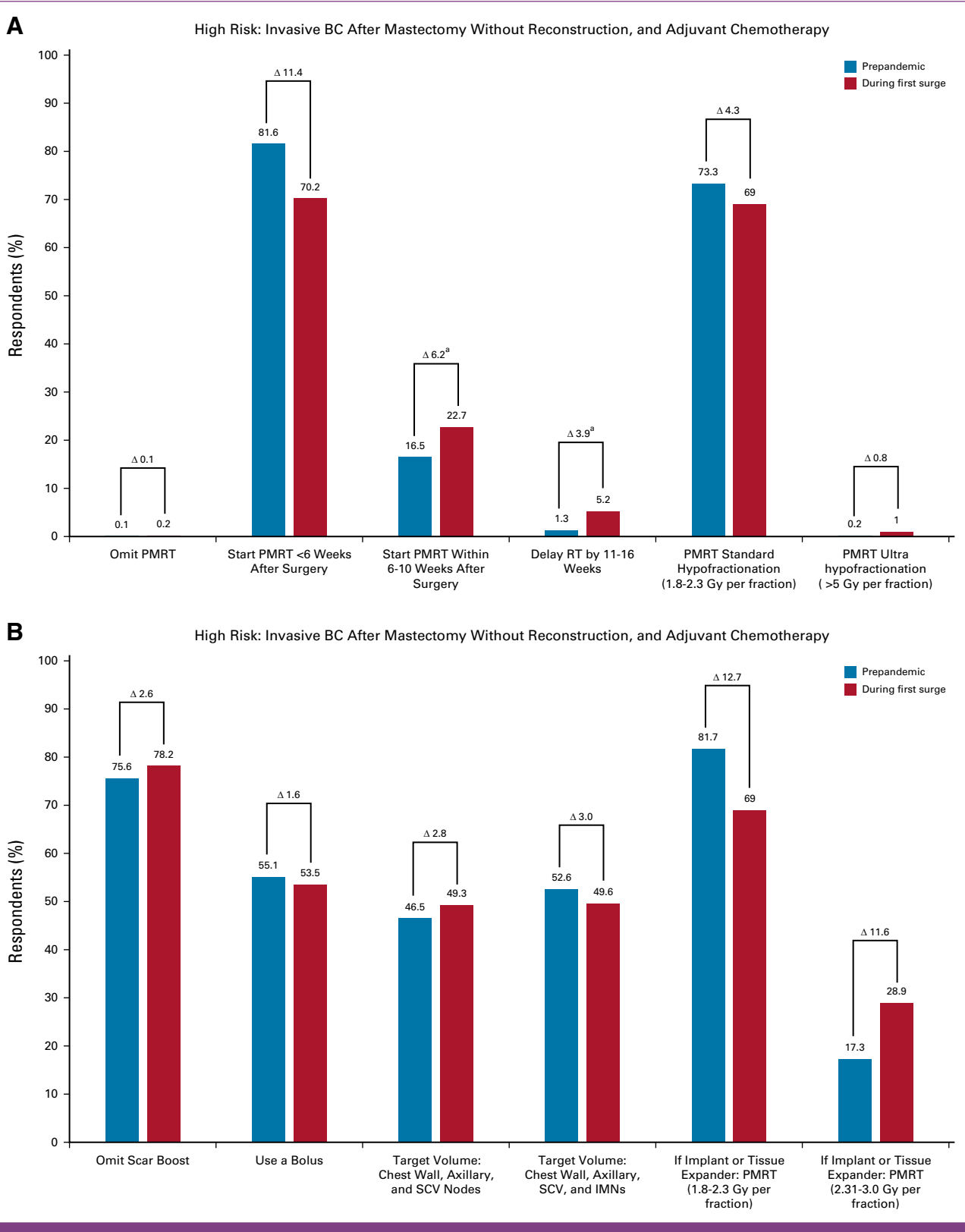
Most (60.3%, n = 665) recommended palliative RT delivered in at least 10 fractions prepandemic, specifically, 50 Gy in 25 fractions (8.1%, n = 89), 45 Gy in 18 fractions (18.7%, n = 206), and 30 Gy in 10 fractions (33.6%, n = 370). However, during the surge, most recommended palliative RT delivered in ≤5 fractions (63.9%, n = 705; P < .0005): 26 Gy in five fractions (18.5%, 204/1,103), 20 Gy in five fractions (26.4%, 291/1,103), and 8 Gy in one fraction (19.0%, 210/1,103).

**DISCUSSION**

Our study is unique in its diverse representation and strong global collaboration between experts reporting treatment recommendations concerning the pandemic’s first surge in their respective nations. It aims to determine whether the pandemic acutely affected practice patterns for patients with BC receiving RT relative to prepandemic times. Participation was robust, with ROs from 54 countries fully completing the survey, demonstrating wide variations in international BC treatment recommendations prepandemic and surge.

In cases 1 and 2, minimal change was observed, with many recommending WBRT delivered with moderate

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**FIG 5.** (A) Distribution of responses on treatment guidelines followed before and during the COVID surge among 1,103 respondents regarding an invasive BC after mastectomy without reconstruction and adjuvant chemotherapy case 5. A 45-year-old woman underwent a left modified radical mastectomy without immediate reconstruction. Pathology revealed a 5-cm grade 2 ER+, PR+, HER- invasive ductal carcinoma with evidence of lymphovascular invasion and five out of 15 positive axillary nodes. She completed adjuvant dose-dense doxorubicin, cyclophosphamide, and paclitaxel. An aromatase inhibitor was planned. (B) Distribution of responses on treatment guidelines followed before and during the COVID surge among 1,103 respondents regarding an invasive BC (continued on following page)



**FIG 5.** (Continued). after mastectomy without reconstruction and adjuvant chemotherapy case 5. A 45-year-old woman underwent a left modified radical mastectomy without immediate reconstruction. Pathology revealed a 5-cm grade 2 ER+, PR+, HER– invasive ductal carcinoma with evidence of lymphovascular invasion and five out of 15 positive axillary nodes. She completed adjuvant dose-dense doxorubicin, cyclophosphamide, and paclitaxel. An aromatase inhibitor was planned. <sup>a</sup>Responses regarding treatment recommendation are shown. BC, breast cancer; ER+, estrogen receptor–positive; HER–, human epidermal growth factor receptor–negative; IMNs, internal mammary nodes; PMRT, postmastectomy RT; PR+, progesterone receptor–positive; RT, radiation therapy; SCV, supraclavicular.

hypofractionation and no boost, prepandemic and surge. Most recommendation changes during the surge indicated delaying, omitting, or abbreviating RT fractionation. This aligned with the HYPO trial publication and published treatment guidelines for physicians prescribing RT during the pandemic,<sup>1,20–25</sup> although the distribution was not uniform. ROs in United States, Saudi Arabia, Canada, and Brazil most recommended delayed RT, while most recommended omitting RT in Russia and Thailand. Similarly, most ultrahypofractionated RT recommendations during the surge were in the United Kingdom, Canada, Spain, and Saudi Arabia. By contrast, respondents in China, United States, South Korea, and Italy infrequently recommended ultrahypofractionation, and some countries did not recommend ultrahypofractionation (Japan, France, and Russia).

Ultrahypofractionated RT for low-risk BC recommendations by ROs in United Kingdom is informed by the FAST trial's 10-year outcomes and FAST FORWARD trial's 5-year outcomes publications,<sup>26</sup> reported during the surge. These showed noninferior outcomes compared with standard fractionation (FAST) or moderate hypofractionation (FAST FORWARD). In United States, where practice patterns can vary significantly by geography and practice type,<sup>27</sup> a notable increase in recommendations for ultrahypofractionated RT for early-stage BC was reported (although lower than in United Kingdom, where practice is uniform with the same dose/fractionation).<sup>28</sup> ROs recommending PBI for early-stage BC favored increasing to  $\leq 5$  fractions during the first surge compared with prepandemic. This change toward accelerated PBI is attributed to the Florence Trial,<sup>29</sup> which published 10-year outcomes during the initial surge and survey period. Its findings demonstrated favorable cosmetic outcomes, similar local recurrence, and similar survival compared with WBRT.

In the first high-risk BC scenario of a patient undergoing mastectomy and sentinel lymph node biopsy with reconstruction for pT2N1 hormone receptor–positive disease, most favored PMRT prepandemic. ROs in Russia and Italy recommended complete axillary dissection prepandemic (a controversial approach since ACOSOG Z11's publication, which provides evidence against such).<sup>30</sup> For this scenario, during the first surge, a notable increase was observed in recommendations for no further local-regional treatment in a pathologically node-positive mastectomy setting. Those favoring complete axillary dissection prepandemic most recommended no further local-regional treatment.

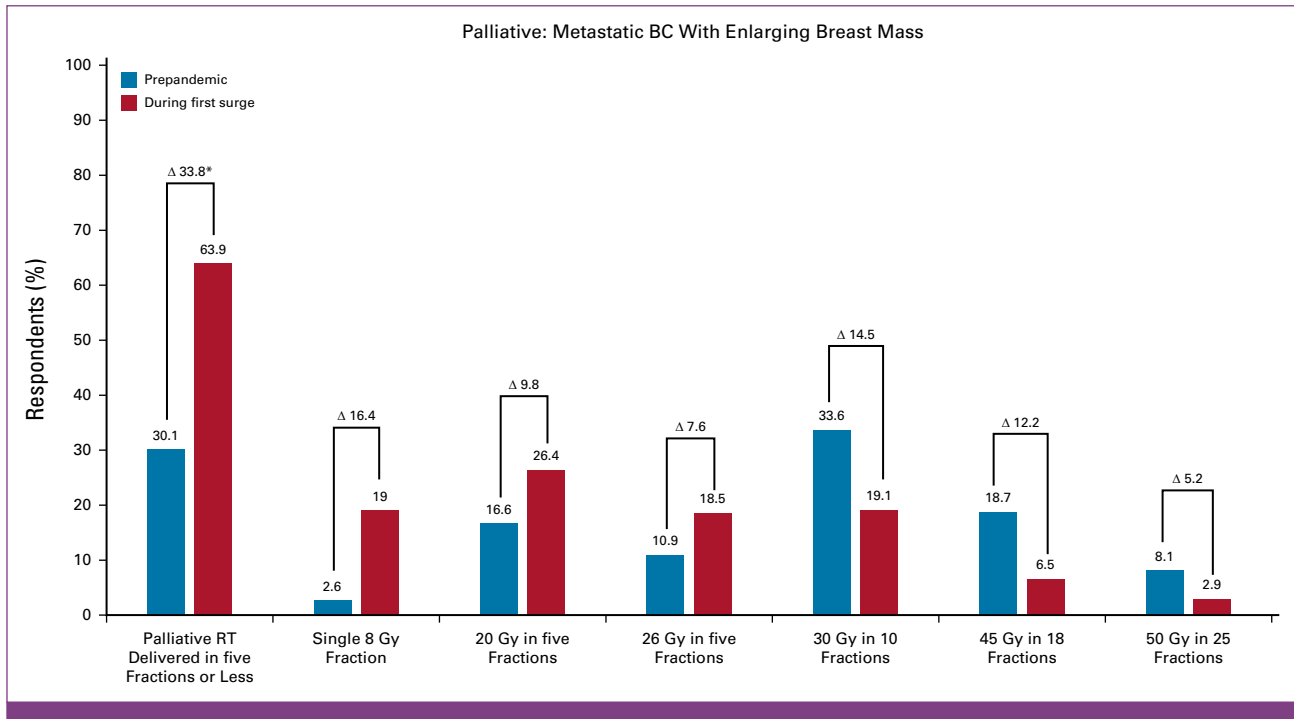
The second high-risk BC scenario of a patient with complete pathologic response in the breast and nodes to NAC

highlights ROs' comfort with moderate fractionation and ultrahypofractionation in the mastectomy setting during the surge. Notably, the willingness to omit postmastectomy radiation in the pathologic complete response setting was observed among 8.4% of respondents prepandemic and increased to 13.1% during the surge.

Although most ROs recommended PMRT delivered in conventional fractionation before and during the surge for patients with high-risk BC, our survey observed a rapid uptake in moderate hypofractionation. Respondents in Canada, Saudi Arabia, Spain, Brazil, and Russia favored moderate hypofractionation, while ROs in United Kingdom mostly recommended ultrahypofractionation. The latter is likely because of United Kingdom oncologists' ongoing experience with patients enrolled in FAST FORWARD's nodal planning study and coordinated breast RT consensus process.<sup>26,28</sup> This comfort with moderate hypofractionation is also likely influenced by a large randomized trial conducted in China<sup>31</sup> comparing conventional fractionation to hypofractionation in the nonreconstructive postmastectomy setting. The long-term results from this trial and findings from similar US clinical trials<sup>32,33</sup> evaluating moderate hypofractionation in the mastectomy setting (including reconstruction) will likely influence widespread global adoption of shorter course treatments. Our survey also revealed that during the surge, recommendations to start PMRT 6–10 weeks after surgery (up to 11–16 weeks) slightly increased compared with typical time frames (within 6 weeks). Notably, for the highest-risk patient with pT3N2 hormone receptor–positive left invasive BC after mastectomy and adjuvant chemotherapy, only half recommended target volumes inclusive of internal mammary nodes (prepandemic and surge), suggesting no worldwide consensus.

In the prepandemic palliative scenario, most recommended palliative RT prescribed in  $\geq 10$  fractions. However, during the surge, most recommended  $\leq 5$  fractions, reflecting a significant change influenced by the pandemic, likely in response to protecting patients from COVID-19 exposure and mindful of their quality of life. Although we cannot assess the economic impact of this by country, it highlights physicians' willingness to recommend shorter treatment courses for terminal BC patients and raises questions about routine practice deficits in nonpandemic periods.

We must acknowledge several limitations in this study. Recall bias and well-documented survey limitations may have affected answers about prepandemic recommendations (such questions referenced practices 7–11 months before



**FIG 6.** Distribution of responses on treatment guidelines followed before and during the COVID surge among 1,103 respondents regarding a metastatic BC with an enlarging breast mass case 6. A 75-year-old woman with metastatic ER+/PR+/HER2- invasive ductal carcinoma resistant to several lines of systemic therapy presented with an enlarging and bleeding 6-cm right breast mass. Her Karnofsky performance status was 80. Surgical resection was not planned because of the presence of multiple lung metastases. \*Responses regarding treatment recommendation are shown. BC, breast cancer; ER+, estrogen receptor-positive; HER2-, human epidermal growth factor receptor 2-negative; PR+, progesterone receptor-positive.

survey distribution). Recall bias may also apply to treatment recommendations for the country-specific surge scenario, which varied among nations and may not have been reached during survey distribution. Additionally, updated treatment guidelines were published during survey distribution, which may have influenced answers. Thus, for the questions related to treatment recommendations during the surge, respondents may have been unable to separate their choice from guideline recommendations. This is salient for hypofractionated RT recommendations during the pandemic's height, as several clinical trials<sup>26,31</sup> validated it, thus making it challenging to attribute recommendation increases to COVID-19 alone.

Another limiting factor is the over-representation of countries with high response rates. Many countries ( $n = 40$ ) had fewer than 25 ROs complete surveys, and 31 had  $\leq 5$  respondents. Additionally, ROs in United States were over-represented (25.8% of respondents), while ROs in Africa were under-represented. We also cannot overlook selection bias because of the unequal response rate, with only 81.3% completing the entire survey. To minimize this, our analysis of country-specific recommendations is

limited to countries with  $>25$  respondents. Finally, each country's culture and its impact on treatment heterogeneity were impossible to factor in.

It is unclear if these recommendations represent lasting changes in BC management 2 years into the pandemic. Nevertheless, as the first of its kind in breast radiation oncology during an unprecedented global health emergency, this survey has numerous strengths, including manifold responses and robust international participation. Historically there have been worldwide differences concerning volume and dose fractionation for BC radiotherapy.<sup>34-36</sup> Our study uniquely provides a snapshot of case-specific treatment recommendations and builds upon published COVID-19-related surveys and experiences.<sup>37-43</sup> Specifically, it demonstrates how the pandemic affected treatment, providing insights into how management varies greatly globally. Lessons gained from this experience will inform consensus guidelines for breast RT and preparedness against future pandemics. Longitudinal surveillance will reveal whether the patterns observed persist after the pandemic and, more importantly, how these changes affect outcomes.

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## DATA SHARING STATEMENT

The authors agree to share anonymized data upon reasonable request by researchers.

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