Local management of second ipsilateral breast cancer events after primary breast-conserving therapy: an international Delphi consensus

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Management of second ipsilateral breast cancer events (iBCEs) remains controversial, and there is a need to collate existing evidence and international guidance on patient selection and local treatment strategies. This project, endorsed by US and European surgical and radiation oncology societies, aimed to gather expert consensus on these issues. A questionnaire on second iBCE local treatment was developed and reviewed by a core group of eight experts, and Delphi methodology was applied over two rounds to 36 panellists, including radiation oncologists, breast surgeons, a plastic surgeon, and medical physicists. Consensus was predefined as agreement of 75% or higher. After two rounds, consensus was reached for 78 (80%) of 97 items. Panellists agreed that patient preferences are central to decision making (100%) and that a second breast-conserving therapy represents a reasonable option for selected patients (100%). Criteria associated with greater suitability for second breast-conserving therapy included an interval between surgeries of at least 60 months, low-risk accelerated partial breast irradiation classification, luminal molecular profile, and no grade 3 late toxicity related to the first breast-conserving therapy. *HER2* (also known as *ERBB2*)-positive or triple negative subtypes were not viewed as absolute contraindications. Strong consensus was also observed regarding the importance of tumour-to-breast volume ratio, clear surgical margins, and tumour bed reirradiation. For patients undergoing mastectomy, immediate autologous reconstruction was preferred (94%) over implant-based approaches (75%). This international Delphi consensus offers structured guidance for the local management of second iBCE and supports shared decision making and individualised treatment planning.

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Introduction

In 2025, there were 2·5 million new cases of breast cancer worldwide, representing approximately 24% of all cancer diagnoses among women.[1] By 2050, this number is projected to rise to 3·6 million new cases annually, underscoring the growing public health impact of breast cancer.[1,2] Over the last three decades, substantial improvements in breast cancer survival have led to a marked increase in the number and prevalence of breast cancer survivors.[3] In view of the rising numbers of long-term breast cancer survivors, a late second ipsilateral breast cancer event (iBCE) represents an increasingly major concern. The 5-year cumulative incidence rate of second iBCE following breast-conserving treatment plus postoperative whole-breast irradiation is approximately 2%, and the 10-year rate is approximately 4%.[4–6] Most breast cancer survivors are at risk of a second iBCE, and numbers will rise in the coming decades, highlighting a substantial clinical challenge.

For patients with a second iBCE after initial breast-conserving therapy, current guidelines recommend salvage mastectomy[7,8] with consideration of a second breast-conserving therapy in selected cases. A phase 2 trial,[9] matched-pair analyses,[10,11] and one systematic review with meta-analysis[12] have reported promising outcomes, supporting a second breast-conserving therapy as a viable alternative for a selected patient population with low-risk second iBCE. Despite these encouraging results, conducting a randomised controlled trial comparing mastectomy with second breast-conserving therapy is likely not feasible. Reluctance of both patients and clinicians to accept random allocation to mastectomy, together with the increasing number of systemic treatment options available at recurrence, would require a prohibitively large sample size for a randomised comparison of these approaches.[13] In this context, structured consensus methodologies could provide a pragmatic approach to guide clinical decision making.

The aim of this international, multidisciplinary Delphi consensus is to provide clinical recommendations on the local management of patients with a second iBCE. By integrating the best available evidence with multidisciplinary expert input, it aims to provide guidance in the absence of a robust level of evidence, supporting patient-centred decision making and optimising local treatment strategies without compromising oncological outcomes or quality of life.

Methods

Expert panel selection

Invitations outlining the study aims and participation requirements were sent to nine presidents of surgical and radiation oncology societies from Europe and the USA: the European Society of Surgical Oncology (ESSO), European Breast Cancer Research Association of Surgical

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Trialists (EUBREAST), the European Association of Surgical Oncology and Plastic Surgery (EASAPS), the American Society of Breast Surgeons (ASBrS), the Society of Surgical Oncology (SSO), the European Society for Radiotherapy and Oncology (ESTRO), the Groupe Européen de Curiethérapie - European Society for Radiotherapy and Oncology (GEC-ESTRO), the American Society for Radiation Oncology (ASTRO), and the American Brachytherapy Society (ABS). Each president nominated experts with established expertise in the therapeutic management of second iBCE, identified through leadership roles in national or international professional societies, relevant peer-reviewed publications, and recognised clinical expertise, resulting in a panel of 38 specialists (figure 1A).

Each society appointed one representative as the primary liaison with ABS and ASTRO sharing a representative; these eight representatives formed the Delphi core group (a multidisciplinary group of breast and plastic surgeons and radiation oncologists), responsible for communication, coordination, and guiding the consensus process. The full panel completed all rounds anonymously via a secure online platform, to minimise the influence of dominant individuals. Participation in the two rounds was required for inclusion in the analysis. Participation was voluntary, and all panellists provided informed consent electronically before enrolment. The panel composition was approved by the ESTRO Guideline Committee.

Questionnaire structure

The questionnaire was developed and overseen by the core group of international experts in second iBCE management (ITR, RDM, JG, JAM, FMD, YZ, BA, and J-MH-L). A second iBCE was defined as a biopsy-proven event after initial breast-conserving therapy, which included lumpectomy, surgical axillary evaluation (for invasive carcinoma), and postoperative whole-breast

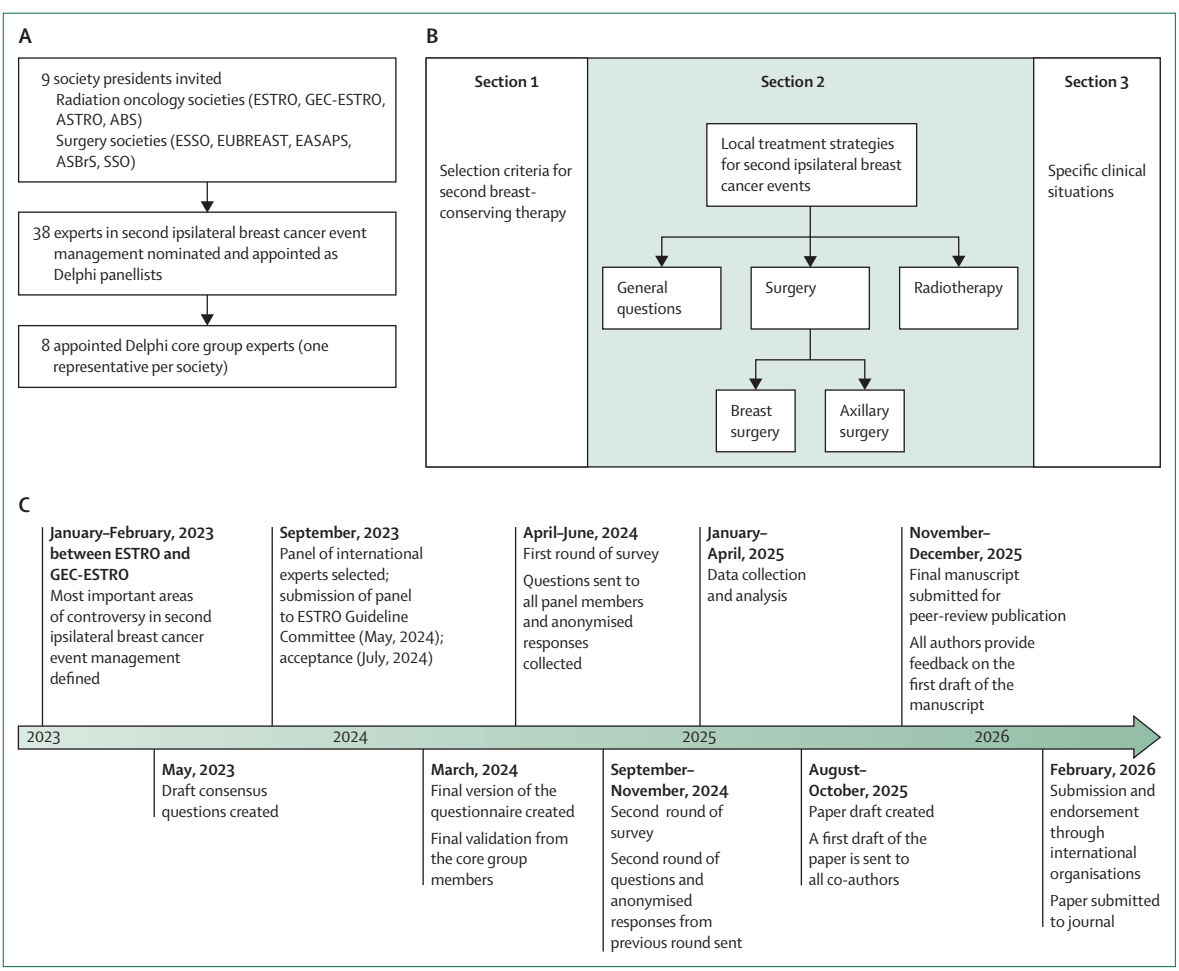

Figure 1: **Overview of the Delphi consensus process**
(A) Panel and core group selection. (B) Structure of the Delphi questionnaire. (C) Timeline of the Delphi process. ABS=American Brachytherapy Society. ASBrS=American Society of Breast Surgeons. ASTRO=American Society for Radiation Oncology. EASAPS=European Association of Surgical Oncology and Plastic Surgery. ESSO=European Society of Surgical Oncology. ESTRO=European Society for Radiotherapy and Oncology. EUBREAST=European Breast Cancer Research Association of Surgical Trialists. GEC-ESTRO=Groupe Européen de Curiethérapie - European Society for Radiotherapy and Oncology. SSO=Society of Surgical Oncology.

irradiation, with or without adjuvant systemic therapy. The core group did not differentiate between true local recurrence and new primary second iBCE, acknowledging that no clear consensus currently exists in this area.[14] Patients with metastatic disease and skin tumours were excluded. For some specialty-specific items, additional experts joined the core group to refine and optimise the relevance of the questions. All core group members also participated as respondents. The initial questionnaire comprised three sections: selection criteria for second breast-conserving therapy; general questions on local treatment, breast and axillary surgery, and radiotherapy; and specific clinical scenarios (figure 1B). Final validation followed three iterative revisions by the core group (appendix pp 2–6).

Delphi process

This study followed a modified Delphi methodology, as recommended in methodological reviews of consensus techniques.[15,16] The core group developed the study protocol and supervised the process. The study workflow is presented in figure 1C. A standardised clinical framework was provided to all panellists to ensure consistency; the index patient was assumed to have been treated with lumpectomy and whole-breast irradiation for the first iBCE, with no grade 3 or worse late toxicities, no treatment-limiting comorbidities, and unrestricted access to diagnostic and therapeutic procedures and systemic therapies. Panellists were instructed not to consider cost, reimbursement, or treatment availability in their responses. Abstention was permitted in cases of insufficient expertise, relevant conflicts of interest, or other justifiable reasons; abstentions were excluded from denominators in the analysis (appendix p 7).

The questionnaire was implemented by means of a cloud-based survey software and two rounds of responses were collected and analysed with controlled feedback after each round, to progressively refine expert opinion. In round one, items were initially single-response, typically binary (yes or no), or numerical. At the start of the second round, panellists received anonymised feedback on group results together with a reminder of their own previous responses. Between the first and second Delphi rounds, items were revised, removed, or refined based on the level and dispersion of consensus, their clinical relevance to the most frequent scenario of second iBCE after previous breast-conserving therapy, and the need to clearly define patient selection criteria for second breast-conserving therapy. Items addressing potential contraindications to a second breast-conserving therapy were reformulated to better reflect clinical nuance and were evaluated using a three-level scale (absolute contraindication, relative contraindication, or no impact). For analytical purposes, relative contraindications and items considered to have no impact were grouped together, allowing clearer identification of situations representing true contraindications, while preserving flexibility for multidisciplinary discussion and shared decision making with the patient when consensus was reached. 14 meetings were organised (ten online, two in person, and two hybrid; appendix p 7).

Two multidisciplinary professional groups in surgery and radiation oncology participated, both responding to questions relating to selection criteria and specific clinical situations, but each responding mainly to discipline-specific items. Full anonymisation across the panel was not feasible, as non-response to some items inherently revealed professional category; this limitation is recognised in multispecialty Delphi designs.[17,18] At the time of analysis, anonymity was maintained within each subgroup, and responses were scrutinised in aggregate.

Before initiation of the Delphi process, all panellists completed a standardised declaration of potential conflicts of interest. These disclosures were reviewed and validated by the core coordinating group (appendix pp 8–9). As the study did not involve patient data, it was exempt from institutional ethics board approval. The study manuscript was reviewed by external specialists recommended by the ESTRO and GEC-ESTRO, ASTRO, ABS, ASBrS, EASAPS, ESSO, EUBREAST, and SSO committees for endorsement purposes, and its final version was approved by all authors.

Literature review

Two complementary literature reviews were conducted. First, a systematic review was undertaken to assess second breast-conserving therapy as an alternative to mastectomy for managing second iBCEs, focusing on comparative oncological outcomes. Specifically, this review aimed to establish whether the oncological outcomes of local treatment for second iBCE differ between mastectomy and second breast-conserving therapy. The search strategy combined the MeSH terms "breast cancer" OR "breast neoplasm" OR "breast carcinoma" AND "ipsilateral recurrence" OR "local recurrence" OR "local relapse" AND "mastectomy" AND "second breast-conserving treatment" and was applied in PubMed and MEDLINE between Jan 1, 1995, and Dec 31, 2025. Eligible studies included original articles and reviews reporting oncological outcomes and prognostic factors related to second breast-conserving therapy after second iBCE as well as comparative studies between mastectomy and second breast-conserving therapy. Second, given the heterogeneity and scarcity of evidence regarding patient selection criteria for a second breast-conserving therapy, as well as the therapeutic strategies encompassing breast and axillary surgery, radiotherapy, and specific clinical scenarios, a narrative literature review was conducted for each of these domains and complemented by an expert consensus derived from a Delphi process.

Data analysis

Descriptive statistics (percentage agreement) were used to summarise item ratings across all rounds. Consensus

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See Online for appendix

proportions were calculated for each statement, and changes in distribution across rounds were analysed to identify shifts in expert opinion. Consensus was predefined as at least 75% agreement, and strong consensus as at least 90% agreement.[19] Only items reaching positive consensus (≥75% agreement) are reported in this Policy Review. The complete set of items, including those with no consensus is provided in the appendix (pp 2–6). Items with three response categories (absolute, relative, or no contraindication to a second breast-conserving therapy) were dichotomised, with absolute contraindication considered as a positive response. Relative and no contraindication were grouped as non-supportive responses, enabling consistent application of predefined consensus thresholds. Full distributions across the three categories are reported in the appendix (p 10).

In addition to global analyses, an exploratory comparative study was performed to assess potential differences between radiation oncologists (n=17) and surgeons (n=19) across the 52 items unrelated to treatment (ie, selection criteria for second breast-conserving therapy and specific clinical situations). For each item, subgroup support rates were calculated with 95% Wilson CIs, and effect sizes were expressed as Cohen's *h*. Differences were tested using two-proportion *z* tests, with statistical significance set at p<0·05. This exploratory analysis was intended to assess consistency across disciplines rather than to establish definitive subgroup effects.

Findings

Panel participation and characteristics

36 (95%) of 38 invited experts completed both Delphi rounds. The characteristics of the responders are reported in the appendix (pp 11, 12). The interdisciplinary panel comprised 21 (58%) women and 15 (42%) men, including 19 surgeons (53%, 18 breast surgeons and one plastic surgeon), 13 (36%) radiation oncologists, two (6%) clinical oncologists, and two (6%) medical physicists. Panellists represented nine countries across Europe (including the UK and Israel) and the USA. 29 (81%) were based at comprehensive cancer centres or academic hospitals. All participants were recognised experts and leaders in breast cancer management. The following results summarise consensus levels across the 97 questionnaire items, organised by patient selection, treatment strategies, and specific clinical situations.

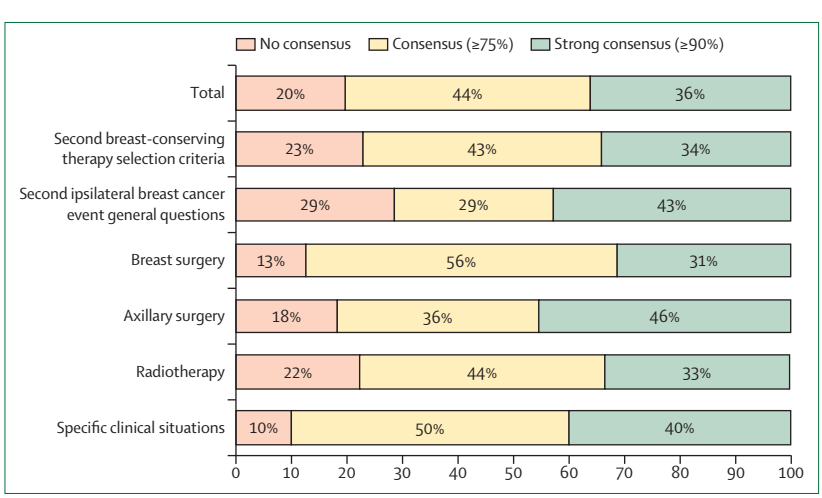

Figure 2: **Consensus distribution across Delphi domains**
Proportions of items reaching no consensus (<75%), consensus (≥75%), and strong consensus (≥90%) are shown for each questionnaire domain and overall.

Overall consensus outcomes

Across both Delphi rounds, 97 items were evaluated. Consensus was achieved for 78 (80%) items and 35 (36%) reached strong consensus. There were 19 (20%) items without consensus. The distribution of consensus levels is illustrated in figure 2 and the appendix (p 13). After round one, 48 (45%) items without consensus were selectively carried forward. Under the guidance of the core group, ten items were removed and 22 were rephrased, leaving 38 items to be reassessed in round two. This iterative process refined the questionnaire and strengthened the robustness of the final consensus (appendix pp 14, 15). The exploratory comparative analysis between surgeons and radiation oncologists confirmed a high degree of concordance between the two specialties (appendix pp 16–20). Consensus outcomes are further detailed by thematic domain.

Domain-specific results

Patient selection

Consensus was reached on 27 (77%) of 35 items regarding patient selection for a second breast-conserving therapy (table 1; appendix pp 21–22). Panellists concurred that a second breast-conserving therapy might represent an appropriate salvage strategy, with tumour-related and breast-related characteristics serving as the main selection criteria, rather than patient age. Consensus highlighted the importance of the interval between the initial cancer and the second iBCE, tumour size (no discriminating threshold could be identified between 36 and 60 months or 20 and 30 mm respectively), tumour-to-breast volume ratio, surgical margins, histoprognostic factors, risk score (named TAM: score based on the combination of time interval [T] between first and second surgery and use of accelerated partial breast irradiation [A] and molecular [M] classifications), and absence of severe late toxicities related to the first breast-conserving therapy. Premenopausal status, and *HER2*-positive or triple-negative subtypes were not considered absolute contraindications provided other criteria were favourable.

Investigations and treatment

Consensus was reached on five (71%) of seven general questions (table 2). Panellists agreed that both axillary imaging and distant staging investigations should be included in the pretreatment investigations for a second

	Yes	No
(1) In the case of second iBCE, is salvage mastectomy considered as the only standard treatment?	0 (0%)	36 (100%)
(2) In the case of second iBCE, could a second BCT be presented to the patient as a valuable or reasonable salvage therapeutic option?	35 (100%)	0 (0%)
(3) Is age ≤40 years at the time of the first breast cancer a contraindication for a second BCT?	5 (14%)	30 (86%)
(5) Is premenopausal status a contraindication for a second BCT?	2 (6%)	32 (94%)
(6) Is TI_{S1S2} a key factor for discussing a second BCT?	31 (89%)	4 (11%)
(8) In general, are adverse histoprognostic factors of the primary breast cancer a contraindication for a second BCT?	4 (12%)	30 (88%)
(9) Is multifocality (tumours located within the same quadrant) a contraindication for a second BCT?	8 (24%)	26 (76%)
(10) Is multicentricity (residing in different quadrants) a contraindication for a second BCT?	29 (81%)	7 (19%)
(11) Is a high tumour to breast size ratio a key factor for discussing a second BCT?	32 (89%)	4 (11%)
(12) Is tumour size of the second iBCE a key factor for discussing a second BCT?	30 (86%)	5 (14%)
(14) Are surgical margins of invasive carcinoma obtained after a second lumpectomy a key factor for discussing a second BCT?	31 (94%)	2 (6%)
(15) Are surgical margins of in situ components obtained after a second lumpectomy a key factor for discussing a second BCT?	28 (88%)	4 (13%)
(16) Are the histoprognostic factors of the first iBCE a key factor for discussing a second BCT?	2 (6%)	33 (94%)
(17) Is an associated extensive intraductal component of a second BCT a key factor for discussing a second BCT?	25 (76%)	8 (24%)
(18) Is infiltrating the extensive lobular carcinoma histological type of the second cancer a key factor for discussing a second BCT?	25 (76%)	8 (24%)
(19) Assuming that all other demographic and histoprognostic factors are favourable, do you consider a second BCT for a poorly differentiated tumour?	25 (76%)	8 (24%)
(22) Assuming that all other demographic and histoprognostic factors are favourable, do you consider a second BCT in case of high Ki-67?	27 (82%)	6 (18%)
(23) Assuming that all other demographic and histoprognostic factors are favourable, do you consider a second BCT in case of *HER2* overexpression?	29 (85%)	5 (15%)
(24) Assuming that all other demographic and histoprognostic factors are favourable, do you consider a second BCT for a triple-negative second iBCE, occurring 10 years after the first iBCE?	27 (82%)	6 (18%)
(25) Is a patient with a second iBCE and a high-risk or cautionary APBI (GEC-ESTRO/ASTRO) classification a contraindication for second BCT?	6 (19%)	25 (81%)
(28) Is the use of PBI classification, molecular classification, and TI_{S1S2} an acceptable manner to determine a good candidate for second BCT?	26 (94%)	1 (6%)
(29) Is a woman presenting with a second iBCE who is postmenopausal, tumour size ≤20 mm, hormone receptor-positive, *HER2*-negative, with a TI_{S1S2} ≥60 months a good candidate for a second BCT?	33 (100%)	0 (0%)
(30) Is the GEC-ESTRO TAM score acceptable for defining second iBCE candidate risk groups as good, grey zone, or bad candidates for second BCT?	20 (95%)	1 (5%)
(31) Are potential late toxicities or sequelae of the first BCT a key factor for discussing a second BCT?	34 (97%)	1 (3%)
(32) Are grade 2 first BCT-related late toxicities a contraindication for a second BCT?	3 (9%)	30 (91%)
(34) Is cosmetic outcome after the first BCT a key factor for discussing a second BCT?	33 (92%)	3 (8%)
(35) Is breast volume at the time of second iBCE a key factor for discussing a second BCT?	33 (92%)	3 (8%)

Data are absolute, with percentages accounting for absentions from some panelists. APBI=accelerated partial breast irradiation. ASTRO=American Society for Radiation Oncology. BCT=breast-conserving therapy. iBCE=ipsilateral breast cancer event. GEC-ESTRO=Groupe Européen de Curiethérapie - European Society for Radiotherapy and Oncology. TAM score=score based on time interval (T) between first and second surgery and use of APBI (A) and molecular (M) classifications. TI_{S1S2}=time interval between first and second BCT.

Table 1: **Consensus responses on patient selection criteria for second BCT**

iBCE. Clinical and radiological surveillance after a second breast-conserving therapy should mirror that recommended after initial breast-conserving therapy. Strong consensus also supported the use of germline genomic testing in patients younger than 40 years at the time of the second iBCE (appendix p 23).

Consensus was reached on 14 (88%) of 16 items related to breast surgery. Panellists agreed that patient preference, age, and life expectancy, as well as cosmetic outcomes after the first breast-conserving therapy, should guide surgical decision making. Fibrosis after the first breast-conserving therapy was also considered an important factor that could prohibit retreatment. Appropriate oncoplastic approaches were endorsed as surgical techniques, when judged appropriate, for repeat lumpectomy. For salvage mastectomy, consensus supported the safety and feasibility of immediate reconstruction (autologous or implant-based), nipple-areolar complex sparing procedures, and fat grafting. Complication rates after mastectomy without reconstruction for second iBCE were judged to be similar to those reported after initial mastectomy, but higher after reconstruction (autologous or implant-based; appendix pp 23, 24).

Consensus was achieved on nine (82%) of 11 items related to axillary management. Panellists agreed that axillary treatment for a second iBCE should be influenced by both the initial axillary procedure and the patient's age or life expectancy. There was strong support for sentinel lymph node biopsy (SLNB) in patients with invasive second iBCE without previous axillary investigation, and for repeat SLNB even in those previously staged with SLNB, provided nodes were clinically negative. Preoperative lymphoscintigraphy was also considered appropriate in this context. Axillary radiotherapy as a substitute for staging, or systematic axillary dissection after a previous SLNB, were not endorsed. Detailed results are available in the appendix (p 24).

Consensus was reached on 14 (78%) of 18 items related to reirradiation strategies. Panellists strongly endorsed

	Yes	No
General questions (5 items)		
(37) Is an axilla ultrasound or MRI mandatory in the second iBCE pretreatment investigations?	27 (77%)	8 (23%)
(38) Are pretreatment distant metastatic investigations mandatory in the second iBCE?	27 (79%)	7 (21%)
(39) Is clinical surveillance after the second BCT the same as that performed after the first BCT?	32 (100%)	0 (0%)
(40) Is radiological surveillance after the second BCT the same as that performed after the first BCT?	33 (100%)	0 (0%)
(41) In the case of a second iBCE occurring in a patient younger than 40 years, are germline genomic tests recommended?	33 (94%)	2 (6%)
Breast surgery (14 items)		
(43) Does patient preference influence salvage breast surgery?	36 (100%)	0 (0%)
(44) Do age or life expectancy influence surgical options for a second iBCE?	27 (77%)	8 (23%)
(45) Is A cup breast size at the time of second iBCE a contraindication for a second BCT?	4 (12%)	29 (88%)
(46) If the first and second iBCEs are in (or close to) the same quadrant, is this a contraindication for a second BCT?	0 (0%)	35 (100%)
(47) Does fibrosis related to the first BCT matter?	31 (89%)	4 (11%)
(48) Does the cosmetic status after the first BCT influence surgical options for a second iBCE?	33 (97%)	1 (3%)
(49) In the case of salvage mastectomy, is immediate reconstruction with autologous reconstruction reasonable?	29 (94%)	2 (7%)
(50) If a salvage mastectomy is planned, is immediate implant-based reconstruction reasonable?	24 (75%)	8 (25%)
(51) In the case of salvage mastectomy, is nipple-areolar complex sparing mastectomy reasonable?	27 (87%)	4 (13%)
(53) In the case of salvage mastectomy, is delayed reconstruction with implant reconstruction preferable?	4 (15%)	23 (85%)
(54) In case of salvage mastectomy, is fat grafting an option?	21 (78%)	6 (22%)
(56) Are complication rates after salvage mastectomy with implant-based reconstruction performed for second iBCE higher compared with the complication rates observed after mastectomy with implant-based reconstruction achieved for first iBCE?	24 (86%)	4 (14%)
(57) Are complication rates after salvage mastectomy with autologous breast reconstruction performed for second iBCE higher compared with the complication rates observed after mastectomy with autologous breast reconstruction performed for first iBCE?	25 (93%)	2 (7%)
(58) Is oncoplastic surgery reasonable for repeat lumpectomy?	25 (78%)	7 (22%)
Axillary surgery (9 items)		
(59) Does age or life expectancy influence axillary management in a second iBCE?	29 (83%)	6 (17%)
(60) Does axillary staging of the primary tumour influence axillary management at the time of second iBCE?	26 (79%)	7 (21%)
(62) Should a SNLB be offered to patients with a previous sentinel lymph procedure?	29 (91%)	3 (9%)
(63) Should preoperative lymphoscintigraphy be considered in the case of a second iBCE with clinically negative axillary nodes?	22 (76%)	7 (24%)
(65) Does second iBCE axillary management depend on the axillary treatment performed for the first iBCE?	29 (85%)	5 (15%)
(66) If no axillary investigation has been performed for the first iBCE, do you propose SLNB in case of invasive second iBCE?	34 (100%)	0 (0%)
(67) If no axillary investigation has been performed for the first iBCE, do you propose axillary irradiation in case of an invasive second iBCE without a new axillary investigation?	2 (6%)	30 (94%)
(68) In the event of a SLNB being performed for the first iBCE, do you propose a repeat SLNB in case of an invasive second iBCE?	27 (90%)	3 (10%)
(69) If a SLNB is performed for the primary, do you propose an axillary lymph node dissection in case of an invasive second iBCE?	1 (3%)	30 (97%)
Radiotherapy (14 items)		
(70) In the case of a second BCT, is breast reirradiation recommended?	32 (94%)	2 (6%)
(72) Regarding a second BCT, is partial breast reirradiation a recommended salvage option?	31 (91%)	3 (9%)
(73) In the case of the second BCT, does the reirradiation technique depend on the first BCT irradiation protocol (whole or partial breast irradiation or hypofractionated regimens)?	27 (80%)	7 (21%)
(74) Can the available CTV delineation recommendations for the first BCT be extrapolated to the second iBCE?	16 (76%)	5 (24%)
(75) Can the available CTV dose-constraint recommendations for the first BCT be extrapolated to the second iBCE?	13 (77%)	4 (24%)
(76) Can available OAR dose-constraint recommendations described for the first BCT be extrapolated to the second iBCE?	15 (75%)	5 (25%)
(77) Is the proof level acceptable for using multicatheter interstitial brachytherapy as a reirradiation technique for second BCT?	20 (91%)	2 (9%)
(79) Is the proof level acceptable for using 50 kV x-ray-based intraoperative radiotherapy as a reirradiation technique for second BCT?	3 (13%)	21 (88%)
(81) Is the proof level acceptable for using external beam radiotherapy as a reirradiation technique for the second BCT?	21 (84%)	4 (16%)
(83) Is the proof level acceptable for using proton therapy as a reirradiation technique for second BCT?	2 (9%)	21 (91%)
(84) Is the proof level acceptable for using thermal ablation for second BCT?	2 (8%)	24 (92%)
(85) Is the proof level acceptable for using radiofrequency ablation for second BCT?	0 (0%)	27 (100%)
(86) Is the multicatheter interstitial brachytherapy-based post-reirradiation grade ≥3 late toxicity rate of around 10% acceptable?	19 (79%)	5 (21%)
(87) Is the external beam radiotherapy-based post-irradiation grade ≥3 late toxicity rate of around 10% acceptable?	19 (76%)	6 (24%)

Data are absolute, with percentages accounting for absentions from some panelists. BCT=breast-conserving therapy. iBCE=ipsilateral breast cancer event. CTV=clinical target volume. OAR=organ at risk. SLNB=sentinel lymph node biopsy.

Table 2: **Consensus responses on salvage treatment for second iBCE**

	Yes	No
(89) Is occurrence of a second iBCE with Ki-67 score of over 25% a relative contraindication for a second BCT?	7 (21%)	26 (79%)
(90) Is the occurrence of a second iBCE with a *HER2*-overexpressed molecular profile always a relative contraindication for a second BCT?	6 (18%)	27 (82%)
(91) Is the occurrence of second iBCE in a patient with previous breast augmentation with implants a relative contraindication for a second BCT?	4 (12%)	29 (88%)
(92) Is the occurrence of second iBCE after initial lumpectomy and reconstruction with chest wall perforator flaps a relative contraindication for a second BCT?	4 (14%)	24 (86%)
(93) Is the occurrence of a second iBCE in a preirradiated area for other causes (lymphoma, lung, or oesophageal cancers or contralateral breast cancer with or without internal mammary chain irradiation) a contraindication for a second BCT?	0 (0%)	34 (100%)
(94) Is the occurrence of second iBCE after lumpectomy alone (without breast irradiation) performed for the first BCT an acceptable indication for a second BCT?	34 (100%)	0 (0%)
(95) Is the occurrence of a second iBCE after PBI performed for the first BCT an acceptable indication for second BCT?	32 (97%)	1 (3%)
(96) Is the occurrence of a second iBCE in a specific anatomic area (eg, subclavicular area, outside or close to the irradiated area for the primary breast cancer) an acceptable indication for a second BCT?	28 (88%)	4 (13%)
(97) Is the occurrence of a second iBCE in the context of oligometastatic disease a relative contraindication for a second BCT?	3 (9%)	31 (91%)

Data are absolute, with percentages accounting for absentions from some panelists. BCT=breast-conserving therapy. iBCE=ipsilateral breast cancer event. PBI=partial breast irradiation.

Table 3: **Consensus responses on specific clinical situations**

breast reirradiation as a recommended component of salvage treatment after second breast-conserving surgery, with partial breast techniques favoured in this setting, taking into account the initial irradiation protocol. Agreement was reached that dose constraints and contouring rules from first breast-conserving therapy can be extrapolated to the second setting. Multicatheter interstitial brachytherapy (MIB) was the technique that was considered most acceptable and external beam radiotherapy (EBRT) was regarded as a reasonable alternative, whereas intraoperative x-ray-based irradiation, proton therapy, and ablative approaches (thermal ablation or radiofrequency ablation) were not endorsed. Acceptable rates of late toxicity of grade 3 or worse (around 10%) after brachytherapy or external beam reirradiation were acknowledged (appendix p 25).

Special clinical situations

Consensus was reached on nine (90%) of ten items addressing specific clinical contexts (table 3). A second breast-conserving therapy was not contraindicated in cases with adverse biological profiles (*HER2* overexpression or a high proliferation marker protein Ki-67 score), previous breast augmentation, or previous lumpectomy with chest wall perforator flaps. Panellists agreed that a second breast-conservation therapy is feasible after a first lumpectomy performed without irradiation or after partial breast irradiation. Second breast-conserving therapy was also deemed acceptable in selected cases with tumours located in anatomically challenging areas, occurring within a previously irradiated field for another cancer, or in the context of oligometastatic disease, provided other factors were favourable (appendix p 26).

Discussion

Whether mastectomy provides superior oncological outcomes compared with a second breast-conserving therapy in patients with a second iBCE remains an unresolved and clinically relevant question. Although international guidelines generally recommend mastectomy as the standard approach, a second breast-conserving therapy can be considered in selected cases. However, the available evidence is mainly derived from retrospective and heterogeneous series, and no phase 3 data are currently available to guide clinical decision making. The systematic review of the literature conducted (appendix pp 27, 28) identified studies that compared oncological outcomes after mastectomy or second breast-conserving surgery, including both unadjusted cohort comparisons (15 studies) and propensity score-matched analyses (eight studies). Despite variations in sample size, follow-up duration, and the variable use of breast reirradiation, unadjusted cohorts[20–34] and matched-pair analyses[10,11,35–40] consistently reported no significant difference in overall survival between the two salvage strategies (appendix pp 29, 30). These findings were further supported by three published systematic reviews, including one meta-analysis[12,41,42] that confirmed the absence of any overall survival advantage for mastectomy over second breast-conserving surgery. Taken together, these findings indicate that the type of local treatment for second iBCE does not appear to significantly influence overall survival.

This persistent lack of high-level evidence underscores the uncertainty surrounding the optimal local management of a second iBCE. In light of these limitations, the Delphi process was designed to capture expert agreement regarding the main clinical and technical determinants guiding the indication of second breast-conserving therapy. Among all domains explored, the selection criteria for offering a second conservative approach emerged as the most crucial and consensual issue. There was unanimous agreement that, in the context of second iBCE, salvage mastectomy should no longer be regarded as the only standard of care. The

panel reached full consensus that a second breast-conserving therapy can be proposed as a valid and valuable salvage therapeutic option in appropriately selected patients. Although the time interval between the first and second breast surgeries and tumour size at local recurrence were regarded as major factors, no consensus was reached on the corresponding thresholds. However, time between first and second breast surgeries is a pivotal prognostic parameter. A shorter time interval has been consistently associated with an increased likelihood of metastatic progression,[43,44] with several studies suggesting threshold values between 48 and 60 months.[45,46] Tumour size and histoprognostic factors represent key points for considering a second breast-conserving therapy. The RTOG 1014 phase 2 prospective trial that analysed the effectiveness of second breast-conserving therapy, enrolled patients with tumour size of 2 cm or smaller, mainly with positive hormonal receptors and without *HER2* overexpression.[9] The TAM score recently proposed integrates GEC-ESTRO partial breast irradiation and molecular classifications as well as time interval between the first and second breast surgeries (appendix p 31).[47] Although the panel achieved strong consensus on its use, this agreement was largely driven by radiation oncologists. 15 panellists, including ten surgeons, abstained, which suggests that the TAM score is likely to be useful to collate separate factors known to influence the selection of second breast-conserving therapy, but requires further assessment and wider acceptance. The panellists also reached a strong consensus that late toxicities from the first breast-conserving therapy should represent an essential determinant in the decision-making process. In total, patients with a low-risk TAM score (=3) at the time of the second iBCE—defined by a time between the first and second breast surgeries of more than 60 months, a low-risk APBI classification, with a luminal molecular profile, and who had no grade 3-late toxicity after the first breast-conserving therapy—were considered suitable candidates for a second breast-conserving therapy, as summarised in figure 3. In the GEC-ESTRO second breast-conserving therapy cohort, patients who were low risk (TAM score 3) accounted for approximately 50% of the cohort.[47] For TAM scores of 4–5 (40%), a second breast-conserving therapy could be considered with caution, taking patient preferences into account. Given the scarce data detailing the efficacy of second breast-conserving therapies for patients with TAM scores of at least 6, the potential increase in local recurrence risk needs to be factored into the patients' desire to preserve their breast and systemic therapy should be discussed within a multidisciplinary tumour board.[47]

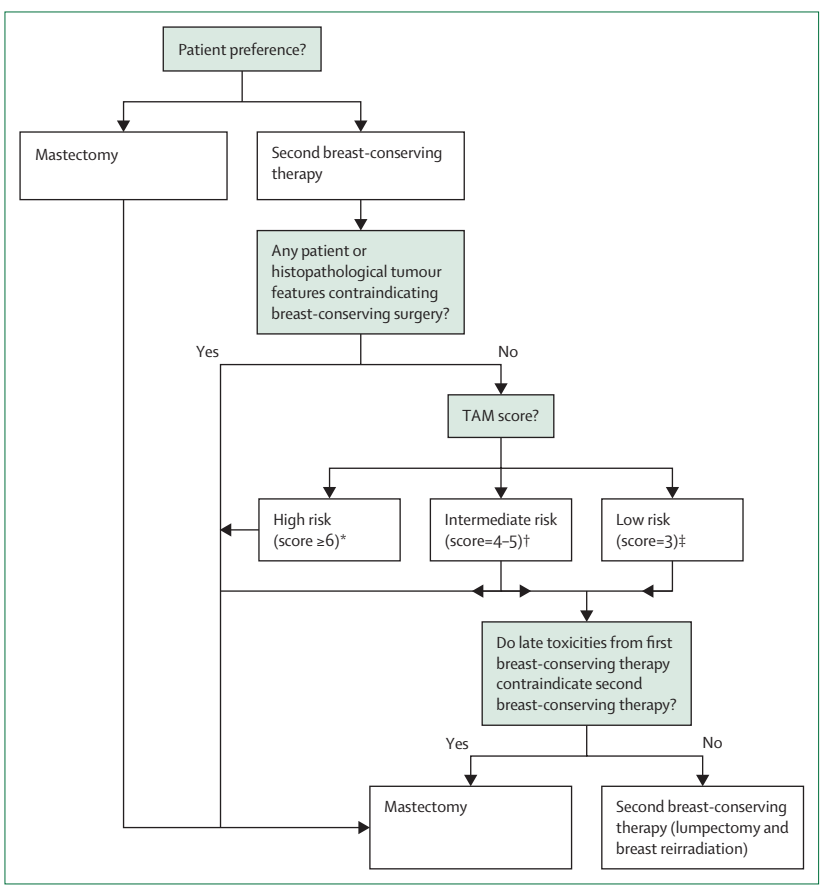

***Figure 3*: Decision pathway for second breast-conserving therapy versus mastectomy in second ipsilateral breast cancer event**

The pathway integrates patient preference, clinical and histopathological contraindications, the TAM score and late toxicities from first breast-conserving therapy to guide selection between second breast-conserving therapy (lumpectomy plus breast reirradiation) and salvage mastectomy. TAM score=score based on time interval (T) between first and second surgery and use of accelerated partial breast irradiation (A) and molecular (M) classifications. *Patients with a TAM score of 3 represent good candidates for a second breast-conserving therapy. †For patients with TAM scores of 4–5, a low risk of unfavourable oncological outcome after a second breast-conserving therapy may be cautiously suggested, although this remains uncertain. ‡For patients with a TAM score of at least 6, mastectomy could be the first therapeutic option. However, a second breast-conserving therapy may be carefully discussed when this therapeutic option is supported by the patient. In such cases, the indication for systemic therapy and appropriate staging investigations should be discussed within a multidisciplinary tumour board.

Panel members agreed that the patient's perspective remains a pivotal consideration among the selection criteria. A recent international survey by our Delphi research group, conducted in partnership with patient advocates, identified key factors supporting informed decision making in this setting. The findings emphasise that when facing a choice between mastectomy and a second breast-conserving therapy, patients require both comprehensive information and adequate time for reflection.[48]

Consensus was reached that pretreatment investigations of second iBCE should include local (breast and axillary) and metastatic assessment. Although MRI can identify additional disease and affect partial breast irradiation eligibility at initial presentation of breast cancer,[49] in the setting of second iBCE, adding breast MRI to mammography and ultrasound improves tumour size estimation and better detects multifocal disease.[50] However, MRI performed after second iBCE diagnosis rarely alters management and should be used selectively,

guided by clinical concern.[51] [18F]fluorodeoxyglucose-PET–CT might be valuable for distinguishing post-treatment fibrosis from viable tumour tissue and for identifying isolated locoregional lesions, including those in aberrant lymphatic drainage areas due to previous surgery or radiotherapy, thereby enabling targeted management.[52] Although PET–CT can influence clinical decisions in approximately 60% of second iBCE cases,[53] its role in the management of local breast cancer recurrences remains a matter of debate and such imaging can be considered in selected patients with local recurrences with unfavourable prognostic features.

Strong consensus was reached that the cosmetic outcome following the first breast-conserving therapy should guide surgical decision making for a second iBCE. Immediate autologous reconstruction after salvage mastectomy was considered a reasonable option; however, complication rates are higher than those observed after autologous reconstruction performed for primary disease. Consensus was also reached that oncoplastic surgery and immediate implant-based reconstruction after mastectomy are reasonable approaches. Data from large-cohort analyses addressing salvage mastectomies and their related complications remain scarce. However, evidence from meta-analyses of randomised controlled trials comparing breast-conserving surgery with mastectomy for primary breast cancer confirms that postoperative skin or flap necrosis occurs significantly more often after mastectomy than after breast-conserving surgery.[54] In the specific context of second iBCE, Elfgen and colleagues[28] reported significantly lower postintervention complication rates after breast-conserving surgery (19·2%) compared with mastectomy (34·3%) or mastectomy with reconstruction (30·8%). Because breast surgery in a previously irradiated breast carries an increased risk of complications, a simple lumpectomy technique is likely to be safer than more extensive oncoplastic approaches in second iBCE surgery.[55,56]

Strong consensus was reached that second SLNB should be offered in patients with a previous sentinel lymph node procedure in case of an invasive second iBCE. Consensus was also reached that axillary staging of the primary tumour influences axillary management at the time of second iBCE. The technical feasibility of performing a second SLNB in the setting of a second iBCE has been shown in individual studies[57–60] and supported by a meta-analysis.[61] However, the influence of a second SLNB on postoperative treatment decisions (including radiotherapy and systemic therapy) as well as its oncological benefit, remains uncertain in clinically node-negative patients.[62–65] In this context, pretreatment PET imaging could potentially assist in selecting patients for whom a second SLNB might be appropriate.[66,67]

The results of this Delphi consensus highlight two key aspects regarding breast reirradiation in the context of a second breast-conserving therapy. First, partial breast reirradiation appears to be an important component of a second conservative treatment strategy. Second, MIB and EBRT using conventional fractionation currently represent the two most established approaches for breast reirradiation. Based on available data, proton therapy, 50 kV x-ray-intraoperative radiotherapy or electron beam-based intraoperative radiotherapy, and radiofrequency ablation were not endorsed for breast reirradiation. Consensus was also achieved that existing recommendations for clinical target volume delineation and organ at risk dose constraints following initial breast-conserving surgery could be extrapolated to the second iBCE. Post-reirradiation grade 3 or worse late toxicity rates of approximately 10% were considered acceptable by the expert panel for both MIB and EBRT. The results of the present analysis are consistent with publications comparing mastectomy with second breast-conserving surgery. In their systematic review and meta-analysis, Tollan and colleagues[12] reported a higher incidence of third iBCE after second breast-conserving surgery, without any difference in overall survival. However, the omission of postoperative breast reirradiation in that analysis limits the interpretation of local control outcomes. In a large matched-pair cohort including 5098 patients, Su and colleagues[11] found increased overall mortality after second breast-conserving surgery alone (hazard ratio 1·64, 95% CI 1·40–1·91; p<0·001), whereas outcomes were comparable to mastectomy when breast-conserving surgery was combined with postoperative reirradiation (HR 1·15, 0·87–1·53; p=0·33). These findings suggest that partial breast reirradiation plays a pivotal role in achieving local and systemic control after a second breast preservation. According to the ESTRO–EORTC consensus, breast reirradiation is now recognised as a type 1 (overlap of irradiated volumes) indication, acknowledging its role as an adjuvant modality.[68–70]

Because of its dose delivery, brachytherapy was the first technique used and reported for breast reirradiation.[71] Early experiences described MIB with low-dose-rate or pulsed-dose-rate schedules, whereas recent studies have favoured high-dose-rate regimens[26,47] (appendix pp 32, 33). EBRT has emerged as a valuable alternative to brachytherapy, initially using three-dimensional conformal techniques and, more recently, intensity-modulated radiotherapy; proton therapy cohorts remain less represented (appendix pp 34, 35).[9,30,33,72] Although standard or hyperfractionated regimens are most commonly applied, moderately hypofractionated schedules have yielded encouraging results.[72] Several prospective trials are currently underway to assess the safety and efficacy of breast reirradiation using standard, moderately hypofractionated, or ultrahypofractionated regimens (appendix p 36). In the setting of ultrahypofractionated regimens, several studies have investigated intraoperative radiotherapy using either 50-kV x-rays or electron beams. However, no consensus

was reached regarding the use of intraoperative radiation therapy as a reirradiation technique, as available results remain immature and suggest a potential increase in complication rates (appendix p 37).[28]

Panellists also addressed specific clinical situations with poor evidence in the literature. Strong consensus was reached that a second iBCE within a previously irradiated area whether after irradiation for other malignancies (eg, lymphoma, lung or oesophageal cancer, or contralateral breast cancer with or without internal mammary chain irradiation), after partial breast irradiation for the first breast-conserving therapy, or in the context of oligometastatic disease, should not be considered a contraindication to a second breast-conserving therapy. Consensus was also reached that a second iBCE with a *HER2*-overexpressing profile, occurring in patients with previous breast augmentation, or in specific anatomical regions (eg, subclavicular area, adjacent to or outside the initial radiation field), represent acceptable indications for second breast-conserving therapy.

Search strategy and selection criteria

The evidence informing this Delphi consensus was based on two complementary literature searches. Two investigators (J-MH-L and FMD) independently conducted a systematic search of PubMed and MEDLINE for articles published between Jan 1, 1995, and Dec 31, 2025, assessing a second breast-conserving treatment as an alternative to mastectomy for local management of second ipsilateral breast cancer events (iBCE). The search combined the MeSH terms "breast cancer" OR "breast neoplasm" OR "breast carcinoma" AND "ipsilateral recurrence" OR "local recurrence" OR "local relapse" AND "mastectomy" AND "second breast-conserving treatment". Eligible studies included original articles, comparative studies, and systematic reviews reporting oncological outcomes, toxicity, or prognostic factors related to a second breast-conserving treatment after a second iBCE. Case reports, studies not specifically addressing local management of a second iBCE, and publications in languages other than English were excluded. Additional relevant studies were identified through manual screening of reference lists and expert cross-referencing and were incorporated when deemed pertinent to the scope of the consensus. 84 studies in the field of second iBCE and second breast-conserving treatment outcome were analysed. Because of the heterogeneity and scarcity of evidence regarding patient selection criteria, surgical management, axillary staging, radiotherapy approaches, and specific clinical scenarios, targeted narrative reviews were conducted within each domain. Reference lists of relevant articles and international guidelines were screened to identify additional sources. The study and its modality were approved by the European Society for Radiotherapy and Oncology Guidelines Committee.

This work is not exempt from limitations. First, no systematic review of the literature was performed across all sections to guide the panellists throughout the questionnaire. As distinction between true local recurrence and an ipsilateral new primary tumour was not possible, a broader definition of second iBCE was adopted. Systemic therapy aspects were not addressed, as the focus was restricted to local management. A key limitation of this work is the absence of randomised or high-level prospective evidence in this clinical setting. As a consequence, the Delphi statements developed here should be interpreted as structured expert consensus rather than formal evidence-based recommendations. As in any consensus process, agreement reflects the expertise and perspectives of the participants, here mainly surgeons and radiation oncologists. Finally, the expressed opinions were largely based on the management of patients from North America and Europe, as not all continents were represented within the experts' pool. Nonetheless, we believe that the systematic methodology and high levels of agreement achieved across an international, multidisciplinary panel provide a robust and transparent framework that can support clinical decision making until stronger evidence becomes available.

Conclusion

This international Delphi study, conducted in collaboration with leading surgical and radiation oncology societies from Europe and the USA, represents the first coordinated effort to establish expert consensus on the local management of second iBCE and to define the role of second breast-conserving therapy with breast reirradiation as a therapeutic option. Patient perspective, TAM score, and grade 3 late toxicity after the first breast-conserving therapy emerged as key determinants when considering second breast-conserving therapy as a reasonable alternative to mastectomy within a treatment de-escalation strategy. However, even in areas in which consensus was achieved, prospective validation through high-level evidence remains warranted. In the absence of randomised or robust prospective data in this clinical setting, the Delphi statements presented here should therefore be interpreted as structured expert consensus rather than formal evidence-based recommendations. Nevertheless, this consensus highlights the importance of comprehensive and balanced patient information to support informed and shared decision making. Ultimately, these expert consensus views aim to support multidisciplinary teams in delivering individualised, patient-centred care for people facing a second iBCE.

Contributors

Conceptualisation: J-MH-L, VS, and PP. Data curation: J-MH-L and FMD. Formal analysis: ITR, RDM, JG, JAM, FMD, YZ, BA, and J-MH-L. Investigation: ITR, RDM, JG, JAM, FMD, YZ, BA, and J-MH-L. Methodology: J-MH-L, VS, PP, and IM. Project administration: ITR, RDM, JG, JAM, FMD, YZ, BA, and J-MH-L. Resources: ITR, RDM, JG,

JM, FMD, YZ, BA, and J-MH-L. Software: J-MH-L and FMD. Supervision: ITR, RDM, JG, JAM, FMD, YZ, BA, and J-MH-L. Visualisation: ITR, RDM, JG, JAM, FMD, YZ, BA, and J-MH-L. Validation: ITR, RDM, JG, JAM, FMD, YZ, BA, and J-MH-L. Writing original draft: J-MH-L, PP, OK-P, IM, and FMD. Writing review and editing: all authors.

Declaration of interests

J-MH-L has received grants or contracts and support for attending meetings and travel from Bayer, Astellas, Elekta. He is president elect of the GEC-ESTRO. JAM is chair of the board for the American Society of Breast Surgeons. MA has received grants from the Engineering and Physical Sciences Research Council (grant number EP/T028017/1) and from The National Institute for Health and Care Research (NIHR) Manchester Biomedical Research Centre (grant number NIH203308) and is a board member of the European Society of Radiotherapy and Oncology. EEB is a site principal investigator at University of Kentucky for an industry-sponsored study looking at a new melanoma gene assay and was an SSO Society of Surgical Oncology Breast Disease Site working group committee member from 2022 to 2024. JdB has received a grant from the Swedish Cancer Society and Swedish Foundation for Strategic Research. IF has received an institutional grant from MSD for a collaboration between MSD and the Karolinska Institutet and is an executive board member of the Swedish Breast Cancer Group and chairman of the Swedish National Breast Cancer Quality Register for Breast Cancer. ODG has received honoraria for lectures from MSD, AstraZeneca, Eli Lilly, BD, Bayer, Applied Medical, and XEOS. JAL is vice chair of the ASTRO Guideline committee. IM has received consulting fees from Menarini StemLine, AstraZeneca, Daiichi Sankyo, Novartis, Eli Lilly, Pfizer, Gilead, MSD, TEMA Sinergie, and Exact Sciences; participated on the data monitoring board for the PARABLE trial (UK); and has leadership positions (uncompensated) with ESTRO (Clinical Board, Breast Focus Group, and Guidelines Sub-Group on Breast member), EORTC (Breast Cancer Group Steering Committee, Radiation Oncology Science Council member), Florence University Hospital, Italy (Head of the Breast Unit). FM has received honoraria for lectures from Elekta. VS has received grants from Elekta, consulting fees and honoraria for lectures from Nucletron an Elekta Company, support for attending meetings from ESTRO, and has a leadership role in the Deutsche Gesellschaft für Radioonkologie, GEC-ESTRO. TK has received honoraria for lectures for MSD, Novartis, Endomag, Sirius Meidcal, AstraZeneca, and Merit Medical; has received support for attending meetings from MSD and Lilly; is chairman of the European Breast Cancer Research Association of Surgical Trialists and co-chairman of Arbeitsgemeinschaft Gynäkologische Onkologie. JV is president of the Dutch Breast Surgeons Working group, a representative in the European Society of Surgical Oncology Educational and Training Committee Breast, on the board of the Nationaal borstkanker overleg Nederland/National breast cancer consultation, and a member of the steering committee for the Breast Cancer Guideline the Netherlands. M-JV-P has received honoraria for lectures to ESSO Gothenborg and is in the ESSO breast advisory group. CY is a board member of the American Society of Radiation Oncology. FMD has a leadership role in the Society of Surgical Oncology. ITR, JG, YZ , OK-P, BA, RDM, DWA, JRD, DD, BG, CG, AK, AM-L, TTN, CP, PP, NR, HS, TS, and SLS declare no competing interests.

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