

# Global variations in the definition and management of multifocal and multicentric breast cancer: the MINIM international survey

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## Introduction

Multifocal and multicentric breast cancers (MFMCBCs) have traditionally been considered a contraindication to breast-conserving surgery (BCS) because of concerns about locoregional control<sup>1</sup>.

The most common definition of MFMCBC is anatomical, based on the presence of cancer foci either in a single breast quadrant (multifocal) or in more than one (multicentric)<sup>2</sup>. Other definitions are based on the distance between tumours, with multifocal tumours defined as being within 2 cm of each other (up to 5 cm in some articles), and multicentric tumours further away<sup>2</sup>.

The reported incidence of MFMCBC varies between 4 and 60 per cent, and has increased, possibly owing to improved imaging accuracy resulting in better detection rates<sup>1–3</sup>. Similarly, BCS rates for MFMCBC have increased over time as a result of the introduction of advanced oncoplastic techniques that allow *en bloc* resection of all cancer foci while preserving (or even improving) breast cosmesis<sup>2–7</sup>. These advances in oncoplastic breast surgery, together with the support of the St Gallen expert panel and emerging evidence of no significant difference in disease-free or overall survival between MFMCBC and unifocal cancers<sup>8–10</sup>, have resulted in changing practice, with many surgeons considering BCS in selected patients<sup>2</sup>. This topic is still, however, debated as other authors have questioned the oncological safety of BCS in this setting because of a lack of RCTs or high-quality prospective cohort studies<sup>4,5</sup>.

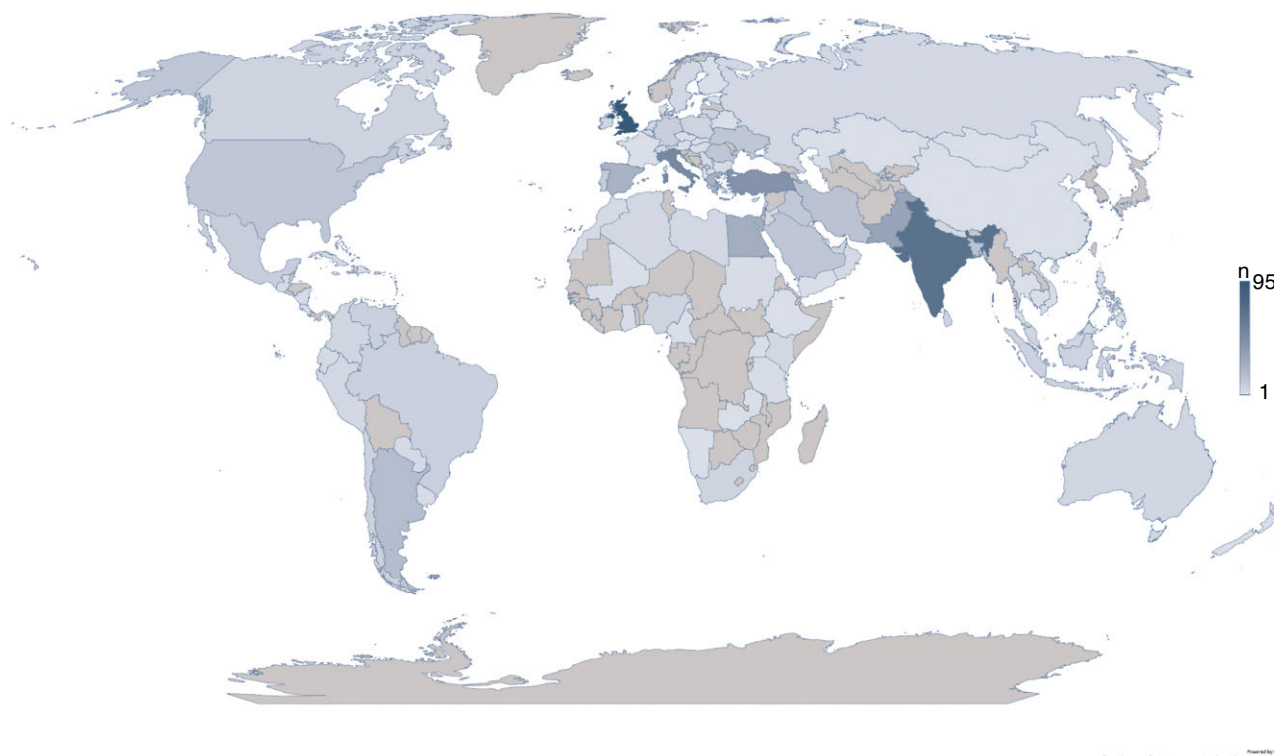
## Methods

The MINIM (MulticeNtrIc Multifocal) survey was designed to understand international variation in the definition and management of MFMCBC. An online questionnaire was developed in REDCap<sup>11</sup> by the authors based on the uncertainties in the literature. The survey consisted of 24 questions divided into five sections (demographics and experience; unit details and cancer workload; definitions; diagnosis; and management). It was piloted and refined iteratively before distribution.

A link to the survey was published on the Group for Reconstructive and Therapeutic Advancements (GReTA) and iBreastBook websites, newsletters, and social media platforms. The online survey was open from 23 July to 6 September 2021.

## Results

A total of 743 physicians from 100 countries responded to the survey (Fig. 1) and 589 (79.3 per cent) completed all the questionnaire domains. The cohort was largely composed of breast surgeons (659, 88.7 per cent) and 482 (64.9 per cent) were experienced clinicians with over 5 years of specialist practice (Table 1). Three hundred and forty-three respondents (46.2 per cent) worked in a unit treating more than 200 new breast cancers per year, and 570 (76.7 per cent) treated both symptomatic and screening patients according to the recommendations of weekly multidisciplinary meetings (Table S1, Figs S1 and S2).



**Fig. 1** Respondents' nation of practice

**Table 1** Respondents' characteristics and clinical experience

|  | No. of respondents<br>(n = 743) |
|--|---------------------------------|
| <b>Sex</b>   |                                 |
| M  | 415 (55.9)                      |
| F  | 327 (44.0)                      |
| Prefer not to say  | 1 (0.1)                         |
| <b>Clinical specialty</b>  |                                 |
| Breast (general surgery background)  | 510 (68.6)                      |
| Breast (obstetrics and gynaecology background)   | 48 (6.5)                        |
| Breast (plastic surgery background)  | 101 (13.6)                      |
| Radiologist  | 9 (1.2)                         |
| Oncologist   | 28 (3.8)                        |
| Pathologist  | 4 (0.5)                         |
| Nurse  | 0 (0)                           |
| Other  | 43 (5.8)                        |
| <b>Clinical role</b>   |                                 |
| Consultant general surgeon with interest in breast   | 226 (30.4)                      |
| Consultant oncoplastic breast surgeon (no general surgery commitments)                                   | 291 (39.2)                      |
| Surgical trainee   | 64 (8.6)                        |
| Senior trainee in last 1–2 years of training (specializing in breast surgery or currently in fellowship) | 53 (7.1)                        |
| Career-grade doctor (associate specialist, Trust grade)  | 38 (5.1)                        |
| Not a surgeon  | 26 (3.5)                        |
| Other  | 45 (6.1)                        |
| <b>Years of specialist practice</b>  |                                 |
| Still in training  | 114 (15.3)                      |
| 0–4  | 146 (19.7)                      |
| 5–9  | 134 (18.0)                      |
| 10–14  | 105 (14.1)                      |
| 15–19  | 75 (10.1)                       |
| ≥ 20   | 168 (22.6)                      |
| Missing  | 1 (0.1)                         |

Values in parentheses are percentages.

Some 422 respondents (56.8 per cent) defined MFMCBC based on the anatomical position of the cancer foci within the breast, whereas only 137 (18.4 per cent) based the different definitions on the distance between cancer foci. Four hundred and thirty-one (58.0 per cent) defined a satellite as a cancer focus located within 5 mm from the main lesion ([Table S2](#)).

There was a trend in favour of the use of BCS for MFMCBC, with 333 respondents (44.8 per cent) considering it in every patient where technically feasible and a further 25.0 per cent who would offer BCS for multifocal, but not multicentric disease ([Table 2](#)). There was variation regarding the use of breast MRI in preoperative planning, with 270 respondents (36.3 per cent) using it in all patients, 253 (34.1 per cent) in selected patients only, and 87 (11.7 per cent) not using it unless indicated otherwise. A common practice for localization of non-palpable tumours was to mark the most peripheral lesions in every direction ([Table 2](#)).

In the event of the incidental finding of a second focus of disease in the excised pathological specimen following BCS for what was initially considered to be a unifocal cancer, when both foci were removed with clear surgical margins, most respondents (482, 62.3 per cent) would consider the surgery complete, irrespective of the distance between the main tumour and the second focus. Similarly, 63.6 per cent of respondents would consider performing margin re-excision in this scenario, in the event of involved surgical margins ([Table 3](#)).

Most respondents (63.1 per cent) reported that they would request receptor status for every focus of cancer present in the resection specimen. Similarly, 494 respondents (66.5 per cent) believed that the choice of adjuvant therapy recommendations should be driven by the features of the most biologically aggressive tumour ([Table 3](#)). Interestingly, most surgeons would not routinely involve a radiation oncologist when planning surgery ([Fig. S3](#)), despite the potential challenges of delivering multiple boost radiotherapy in MFMCBC<sup>12</sup>.

Table 2 Respondents' approach to surgical planning

|   |   | No. of respondents (n = 743) |
|---|---|------------------------------|
| If MFMCBC is diagnosed on triple assessment, what is your surgical approach?                                | BCS is not safe, mastectomy for all patients, will not offer reconstruction   | 23 (3.1)                     |
|   | BCS is not safe, mastectomy for all patients and will offer reconstruction  | 71 (9.6)                     |
|   | Consider BCS only for multifocal but not multicentric disease   | 186 (25.0)                   |
|   | Consider BCS for MFMCBC if technically possible   | 333 (44.8)                   |
|   | Missing   | 130 (17.5)                   |
| If you consider breast conservation for MFMCBC, would you routinely do MRI on all patients?                 | MRI in all patients   | 270 (36.3)                   |
|   | MRI in selected patients only   | 253 (34.1)                   |
|   | Not performed unless there are other indications for MRI  | 87 (11.7)                    |
|   | Missing   | 133 (17.9)                   |
| If you consider breast conservation for MFMCBC, would you localize the non-palpable tumours before surgery? | Most medial and most lateral lesions when tumours are inline; if not, all non-palpable lesions localized            | 173 (23.3)                   |
|   | Localize tumours needed to delineate extent of disease (e.g., most medial, lateral, superior, and inferior aspects) | 300 (40.4)                   |
|   | Every lesion localized even when inline   | 116 (15.6)                   |
|   | Other please specify  | 20 (2.7)                     |
|   | Missing   | 134 (18.0)                   |

Values in parentheses are percentages. MFMCBC, multifocal and multicentric breast cancer; BCS, breast-conserving surgery.

Table 3 Respondents' approach to surgical management and adjuvant treatment selection

|   |   | No. of respondents (n = 743) |
|---|---|------------------------------|
| If you have done BCS for what was thought to be a unifocal tumour and the final histology shows a satellite (small second lesion within 5 mm of index lesion) and both tumours are completely excised, what will your MDT advise? | Mastectomy  | 39 (5.2)                     |
|   | Consider the surgery complete and refer to oncology for further treatment | 526 (70.8)                   |
|   | Other   | 27 (3.6)                     |
|   | Missing   | 151 (20.3)                   |
| If you have done BCS for what was thought to be a unifocal tumour and the final histology shows multifocal disease (second lesion is 1 cm apart) and both tumours are completely excised, what will your MDT advise?              | Mastectomy  | 64 (8.3)                     |
|   | Consider the surgery complete and refer to oncology for further treatment | 482 (62.3)                   |
|   | Other   | 46 (5.9)                     |
|   | Missing   | 151 (19.5)                   |
| If you have done BCS for unifocal tumour and the final histology shows multifocal disease and one of the margins is not clear, what will your MDT advise?   | Mastectomy in all patients  | 99 (12.8)                    |
|   | Re-excise margins in selected patients if technically possible            | 492 (63.6)                   |
|   | Missing   | 152 (19.6)                   |
|   | Other   | 0 (0.0)                      |
| Will your MDT advice be to check receptor status (ER, PR, HER2, Ki-67) for all tumours?   | Yes, for all patients   | 469 (63.1)                   |
|   | Only in selected patients for whom it is felt to be clinically relevant   | 93 (12.5)                    |
|   | No, we check it only for the main tumour                                  | 30 (4.0)                     |
|   | Missing   | 151 (20.3)                   |
| If you have completed your surgery for MFMCBC, your MDT will decide on further oncological treatments based on  | Combining sizes of all tumours  | 41 (5.5)                     |
|   | Based on largest tumour   | 57 (7.7)                     |
|   | Based on more biologically aggressive tumour                              | 494 (66.5)                   |
|   | Missing   | 151 (20.3)                   |
|   | Other   | 0 (0.0)                      |

Values in parentheses are percentages. BCS, breast-conserving surgery; MDT, multidisciplinary team; ER, oestrogen receptor; PR, progesterone receptor; HER2, human epidermal growth factor receptor 2; MFMCBC, multifocal and multicentric breast cancer.

## Discussion

The MINIM survey has evaluated the definition and management of MFMCBC in a large international cohort of experienced breast surgeons. Despite a lack of consensus regarding the definition of MFMCBC, this survey clearly showed that the international breast surgical community is largely supportive of the use of BCS in multifocal and, to a lesser extent, multicentric breast cancer. Multifocal disease discovered after surgery, irrespective of the distance of the secondary foci from the index lesion, was considered by a large proportion of surgeons not to require further surgery if

the margins were clear. Nevertheless, the variation in definitions highlighted by this survey is an important consideration when planning future work, particularly for the selection of appropriate inclusion and exclusion criteria for study participants.

The use of MRI was controversial, with no consensus regarding its use in patients with a biopsy-proven breast cancer, even though there appears to be a trend in favour of its use. Dynamic contrast-enhanced MRI can be more useful than mammography and ultrasound imaging when characterizing the extent of multifocal and multicentric disease in dense breasts or when

extensive ductal carcinoma *in situ* is present<sup>13,14</sup>. Despite the improved preoperative disease assessment, the use of MRI has often not translated into improved surgical outcomes, with studies<sup>15,16</sup> showing conflicting results on the rate of reoperation for positive margins.

Several case series available in the literature have demonstrated a degree of heterogeneity in grade and receptor expression in the context of MFMCBC, even between tumour foci with similar histology<sup>4,17</sup>. The current evidence is reflected in the results of this survey, with respondents indicating that tumour biology should be assessed for all tumour foci, and that the biology of the most aggressive cancer should drive the choice of adjuvant treatments.

This is an international study with a good response rate, but some geographical areas are under-represented, which may have influenced the results. There may have been response bias, with responding surgeons differing in some way from those who did not participate, and it is possible that surgeons' reported practice was not consistent with their actual management of this patient group. This survey did also not consider how, in some low-middle-income countries, the lack of radiotherapy facilities might affect the ability of surgeons to offer BCS, not only for MFMCBC but also for unifocal cancers. Despite these limitations, the present work has provided a clear snapshot of current international practice that can inform future work in this area.

MFMCBC will become increasingly important as more advanced imaging modalities are used. Offering the optimal management for these patients will therefore be vital to improve clinical and patient-reported outcomes. Large-scale international studies including key outcomes are needed, but consensus regarding inclusion and exclusion criteria will be required to optimize the design and conduct of this work.

Disclosure. The authors declare no conflict of interest.

## Supplementary material

Supplementary material is available at *BJS* online.

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