

## TITLE PAGE

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# **A Multicentre Study of the Relationship between Abdominal Flap and Mastectomy Weights in Immediate Unilateral Free Flap Breast Reconstruction and the Effect of Adjuvant Radiotherapy**

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## **SUMMARY**

Abdominal free flaps are considered the gold standard for post-mastectomy autologous breast reconstruction. A key element of outcome assessment is breast symmetry often achieved by approximating the reconstructed breast dimensions such as weight (wt) to those of the mastectomy. However, the ideal relationship between these two entities remains unclear.

525 immediate unilateral abdominal free flap breast reconstruction (FFBR) patients were enrolled in a multicentre study (UK 141; Italy 384) and subdivided into Group A (flap wt < mastectomy wt, n=163), Group B (flap wt > mastectomy wt, n=260) and Group C (flap wt = mastectomy wt, n=102). Their rates of contralateral balancing and ipsilateral revision surgeries were compared using Chi-Square tests. Radiotherapy influence on these adjustment procedures was also assessed.

More contralateral balancing procedures (17%) were performed than ipsilateral revisions (10%). Group A rates of contralateral balancing procedures were three times higher than Group B's with a ratio of 37 to 1 versus Group C (37% vs 11% vs 1% respectively,  $p < 0.001$ ). Similarly, the ipsilateral breast revision surgery rate in Group A was double that of Group B and almost three times that of Group C (17% vs 8% vs 6% respectively,  $p = 0.01$ ). Adjuvant radiotherapy disproportionately increased ipsilateral revisions versus contralateral balancing surgeries ( $p = 0.028$ ).

A flap-to-mastectomy weight ratio of less than 1 (Group A) significantly increases subsequent adjustments on both contralateral and reconstructed breasts whilst irradiation predisposes to ipsilateral revisions. This is important in patient counselling and intraoperative flap contouring. Flap weight should ideally approximate or exceed mastectomy weight in unilateral FFBR.

**Keywords:** Contralateral balancing surgery, ipsilateral revision surgery, breast radiotherapy, flap weights, immediate breast reconstruction, breast symmetry.

## **BACKGROUND**

Breast cancer (at 25%) is the most common malignancy in women worldwide but is responsible for only 14.3% of their cancer deaths. Estimates suggest that in the UK and Italy 1 in 8 women will develop breast cancer in their lifetime. However, amongst all cancer types, breast has the highest survival and cure rates.<sup>1-6</sup> In terms of treatment, around 40% of breast tumours need to be treated by removal of the entire breast (mastectomy) and many of these women perceive this therapeutic procedure to be sufficiently traumatic to request reconstruction.<sup>7-9</sup>

Since breast cancer has a high survival rate and today post-mastectomy breast reconstruction constitutes a well-established component of breast cancer treatment, it is evident that improving reconstruction outcomes is an important on-going oncological goal.<sup>8</sup> The key element of these outcomes is symmetry with the opposite breast and surgeons aim to achieve this objective principally by approximating the dimensions of the reconstructed breast to those of the mastectomy specimen.<sup>10-12</sup>

Because of the limited amount of research dedicated to this area<sup>13-16</sup> and since abdominal free flap breast reconstruction (FFBR) is the best autologous method for it,<sup>6,13,17</sup> we decided to carry out a multicentre study, which compared abdominal free flap weight with mastectomy weight in immediate unilateral FFBR, with the specific aim of elucidating the frequencies of contralateral balancing and ipsilateral revision surgeries according to the relative magnitudes of the mastectomy versus flap weights.<sup>18</sup> The findings might have bearing on pre and postoperative patient counselling and the operating surgeon's intraoperative flap contouring.

The second purpose of the study was to evaluate the influence of adjuvant radiotherapy (RT) on the number of adjustment procedures and, thus, how it (objectively) impacts autologous breast reconstruction.

## **METHODS**

With approval from our Institutional Review Board, patients who underwent immediate unilateral breast reconstruction with abdominal free flaps between May 2004 and August 2018 at one UK and two Italian University Hospitals were enrolled for our multicentre retrospective analytical study. The investigation was carried out at Addenbrooke's Hospital of Cambridge University Hospitals NHS Foundation Trust (Cambridge, UK) and at a joint Italian research centre: the Azienda Ospedaliera Universitaria (AOU) "San Giovanni di Dio and Ruggi d'Aragona" of Salerno and the AOU "Sant'Andrea di Roma".

Patients were identified from the theatre registers and the electronic logbooks of the attending surgeons. Their electronic charts were then reviewed for demographic data, intraoperative details (mastectomy and flap weights) and postoperative outcomes with respect to whether the patient required contralateral balancing surgery or ipsilateral revision surgery to achieve symmetry, with a follow up at least of a year and a half after primary surgery. Patients with bilateral or delayed breast reconstruction or those reconstructed with non-abdominal autologous free flaps were excluded from the study. Patients with incomplete information in our database were also excluded from the study leaving a total of 525 consecutive patients: 141 in the UK arm and 384 in the Italian arm.

The flap and mastectomy weights were measured by the scrub nurses independent of the operating surgeons. Following harvest, the entire flap is weighed and after the microanastomoses, any excess and poorly vascularised tissue is trimmed and subtracted from the "initial flap weight" to leave the "final flap weight" which henceforth with is simply referred to as "flap weight".

For analysis, the patients were then divided into three groups: Group A comprised those with a flap weight less than mastectomy weight (n=163), Group B those whose flap weights

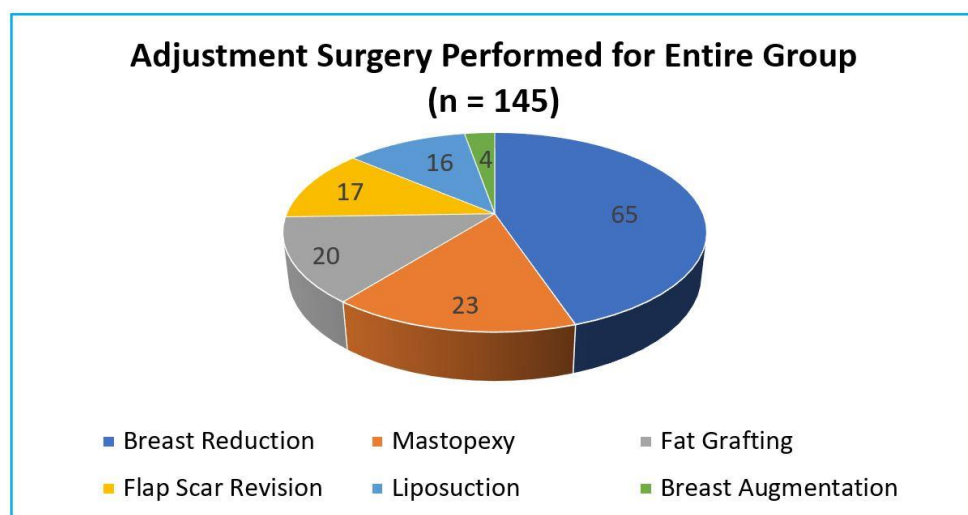
exceeded their mastectomy weights (n=260) and Group C whose flap weight was equal to mastectomy weight (n=102) within +/- 10g of each other. The three groups were then compared with respect to the number of cases requiring contralateral balancing surgery or ipsilateral revision surgery. Radiotherapy influence on the incidence of these adjustment procedures was assessed by comparing the irradiated versus the non-irradiated patients.

*Statistical Methods:* The group rates of contralateral balancing and ipsilateral revision surgeries were compared using the Chi-Square test. It was also used in the radiotherapy subgroup analysis. Continuous variables were analysed using Student's t test. A value of  $p < 0.05$  was considered statistically significant.

## RESULTS

A total of 525 immediate unilateral abdominal free flap breast reconstruction patients (141 from the UK and 384 from Italy) were enrolled in the study. Their average age was 52 years (range, 26 to 78 years) with a mean BMI of 27kg/m<sup>2</sup> (range, 21 to 38kg/m<sup>2</sup>). For the whole group, the average mastectomy weight was 623g (range, 138 to 2100g) while the average flap weight was 635g (range, 220 to 1475g). The number of patients in Group A (flap weight < mastectomy weight) was 163 (31%), in Group B (flap weight > mastectomy weight) was 260 (50%) and in Group C (flap weight = mastectomy weight) was 102 (19%). The median difference between flap and mastectomy weight was 142.5g for Group A, 121g for Group B and 2g for Group C. The groups were comparable in terms of demographic data (age/BMI) and number of patients receiving adjuvant radiotherapy (p>0.05).

Just under one third of all patients (145/525) needed adjustment surgery to achieve symmetry, the details of which are given in Figure 1. Of these almost half (44.8%) underwent breast reduction with the remainder requiring mastopexy (15.9%), fat grafting (13.8%), flap scar revision (11.7%), liposuction (11%) and breast augmentation (2.8%).



**Figure 1:** Pie chart showing types of adjustment surgery undertaken in the entire study group.

Overall, the incidence of adjustment surgery was dominated by contralateral balancing procedures at 17% versus 10% for revisions of the reconstructed breasts ( $p < 0.001$ ). The balancing operations performed on the contralateral breast are shown in Table 1a and were mainly reduction mammoplasties (Figure 2).

<b>Contralateral Balancing Surgeries (n = 91)</b>	
<i>Procedures</i>	<i>Percentage</i>
Breast Reduction	71.4%
Mastopexy	25.3%
Breast Augmentation	2.2%
Fat Grafting	1.1%

**Table 1a:** Frequency of contralateral balancing surgeries for the entire study population.



**Figure 2:** A 55-year-old patient who underwent a left mastectomy (985g) and DIEP flap reconstruction (936g) followed by contralateral T-scar breast reduction (6 months later). Pre-operative (Fig. 2A and C) and 2 years post-operative appearance (Fig. 2B and D). The patient declined nipple reconstruction.

In contrast, adjustment procedures on the reconstructed breasts were more evenly distributed (Table 1b).



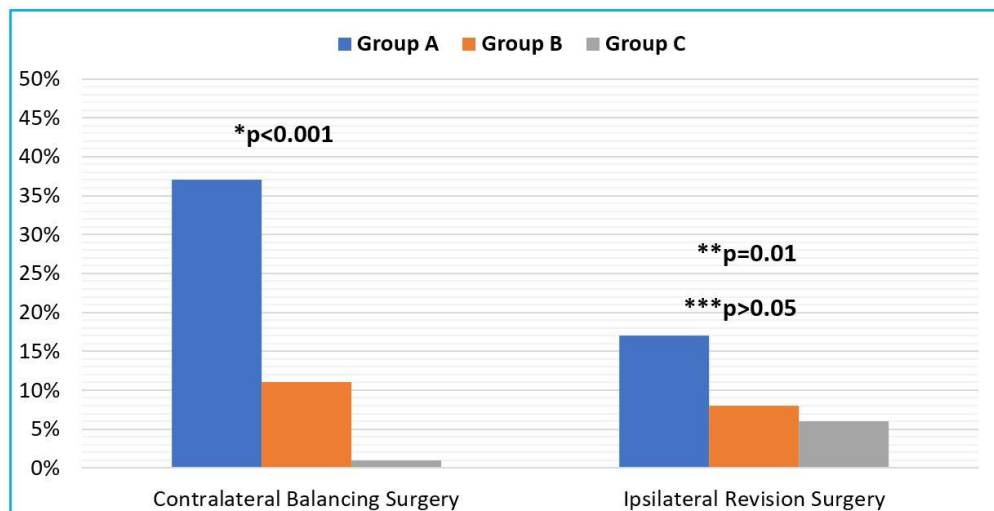
<b>Ipsilateral Revision Surgeries (n = 54)</b>	
<i>Procedures</i>	<i>Percentage</i>
Fat Grafting	35%
Skin Revision	31%
Liposuction	30%
Breast Augmentation	4%

**Table 1b:** Frequency of ipsilateral revision surgeries for the entire study population.

### Comparison

The rate of contralateral balancing procedures needed to achieve symmetry was the highest in Group A at 37% compared to Group B at 11% ( $p < 0.001$ ) and Group C at 1% ( $p < 0.001$ ) [Figure 3] and was also statistically significant when comparing Group B with Group C (11% vs 1%) [ $p < 0.001$ ].

Similarly, the ipsilateral breast revision surgery rate of Group A was double that of Group B (17% vs 8% respectively,  $p = 0.01$ ) and almost three times that of Group C (17% vs 6% respectively,  $p = 0.01$ ) [Figure 3] while there was little difference between Group B and C (8% vs 6% respectively) [ $p > 0.05$ ].



**Figure 3:** Bar chart comparing the frequencies of contralateral balancing surgery for Groups A, B and C ( $*p < 0.001$ ) and ipsilateral revision surgery between Groups A and B ( $**p = 0.01$ ); A and C ( $**p = 0.01$ ) and Group B and C ( $***p > 0.05$ ) [ $\chi^2$  test].

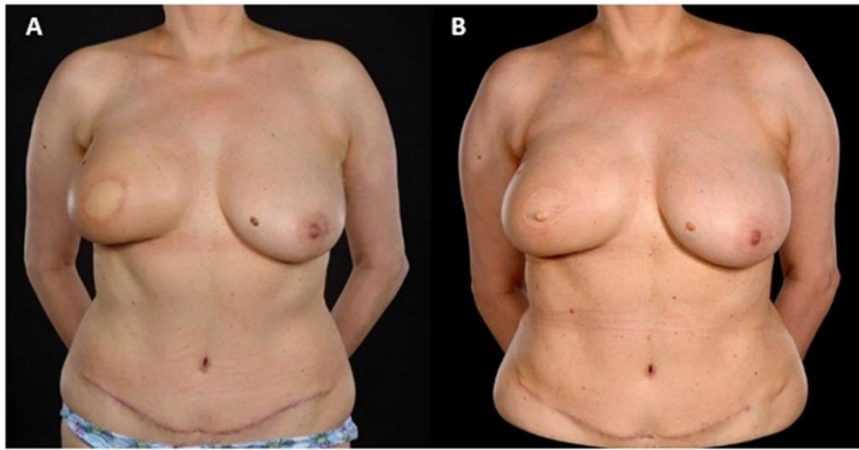
### *Adjuvant radiotherapy*

Of the entire study population, 162 patients (31%) received adjuvant radiotherapy (RT). Of these, 35% needed adjustment (contralateral or ipsilateral) surgery to improve symmetry comprising breast reduction (39%), flap scar revision (25%), mastopexy (16%), fat grafting (14%), liposuction (4%) and breast augmentation (2%) [Table. 2].

<b>Adjustment Surgeries Performed in Irradiated Patients (n = 56)</b>	
<i>Procedures</i>	<i>Number (%)</i>
Breast Reduction	(39%)
Flap Scar Revision	(25%)
Mastopexy	(16%)
Fat Grafting	(14%)
Liposuction	(4%)
Breast Augmentation	(2%)

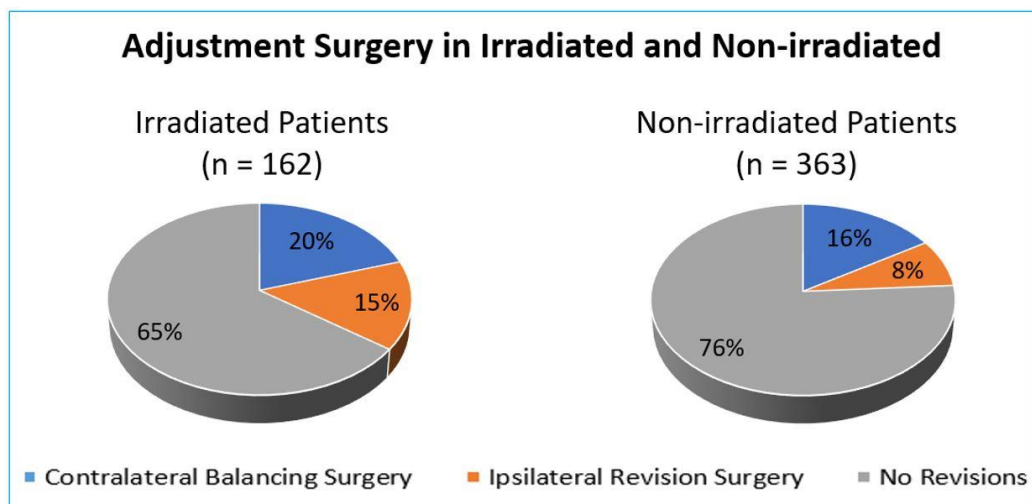
**Table 2:** Frequency of contralateral and ipsilateral adjustment operations (symmetrising and otherwise) performed in the radiotherapy patients.

Adjuvant RT recipients had significantly more adjustment surgeries (35%; 56/162) compared to their non-radiotherapy counterparts (24%; 89/363) [p=0.02]. This was mainly due to the significant difference in the percentage of ipsilateral revision procedures (Figure 4) as it was almost double in recipients of RT (15%) compared to non-recipients (8%) [Figure 5; p=0.028].



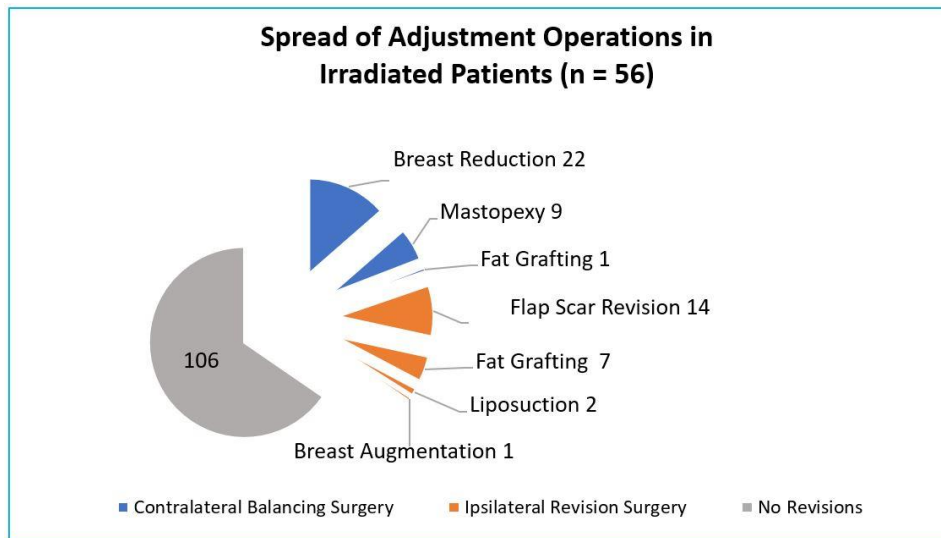
**Figure 4:** A 52-year-old patient who underwent a right mastectomy (mastectomy weight=457g; flap weight=627g) with a contracted misshapen right DIEP reconstruction post-radiotherapy, improved by ipsilateral fat grafting (1 year later) [Fig. B]. 6 months post-operative appearance (Fig. A) and 2 years post-operative (Fig. B).

In contrast, the rates of contralateral adjustment operations in the irradiated and non-irradiated patients were similar (20% vs 16% respectively,  $p>0.05$ ) [Figure 5].

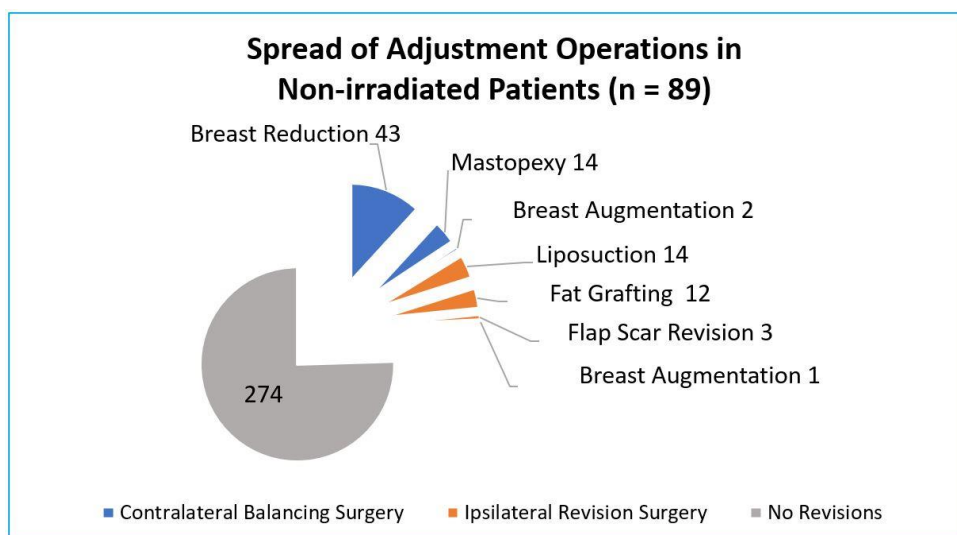


**Figure 5:** Distribution of adjustment surgeries in irradiated and non-irradiated patients. There was only a significant difference in the ipsilateral revision surgeries here shown in orange colour ( $p=0.028$ ,  $\chi^2$  test).

There was a significant difference in the rates of ipsilateral revision surgeries between the two groups (15% vs 8% respectively,  $p=0.028$ ) [Figure 5]. On subgroup analysis the reason for this variance was the different numbers of flap scar revisions (9% irradiated vs 1% of non-irradiated,  $p<0.001$ ; Figures 6 and 7). The detailed distribution of the types of adjustment procedure based on whether the patients had undergone RT or not is shown in Figures 6 and 7.



**Figure 6:** Distribution spread of specific type of adjustment surgeries in irradiated patients.



**Figure 7:** Distribution spread of specific type of adjustment surgeries in non-irradiated patients.

## DISCUSSION

A key element in the assessment of breast reconstruction outcomes is symmetry with the opposite breast. This can be achieved by approximating the dimensions of the reconstructed breast to those of the removed breast (i.e. the mastectomy). Although flap reconstruction easily lends itself to this intraoperatively, it remains undetermined whether the weight of the flap should be bigger, smaller or equal to the mastectomy weight. In order to establish this, we compared the outcomes following immediate unilateral abdominal flap breast reconstructions based on the relationship between mastectomy and free flap weights. This was studied using the objective definitive endpoints of contralateral balancing and ipsilateral revision surgeries with an additional analysis of the effect of radiotherapy. This is a subject which has been scantily addressed in the literature.<sup>15,17,19</sup> Furthermore, complicated formulas proffered for planning and determining reconstructive breast size<sup>20-23</sup> are limited by methodological shortcomings, variable estimations and/or complexity thus rendering them largely impractical for routine clinical use (in busy practices).

The use of objective endpoints for assessing breast reconstruction outcomes provided a useful method for attempting to derive the ideal relationship between flap and mastectomy weight. In general, the lower the rate of adjustment surgery the better the patient-reported-outcome measures (PROMs) as performance of such symmetry surgery is dictated by patient dissatisfaction with the results culminating in patient requests for revision surgery. Measuring breast weights and mastectomy weights is simple, reproducible, practical and dependable. It is also routinely undertaken in most microvascular practices and does not increase the operation length or endanger the flap surgery. Additionally, in the series herein reported the flap and breast weights were not influenced by the operating surgeons as they were measured by the theatre nurses independent of the surgeons.

Our study demonstrated that when the flap weight was less than the mastectomy weight there was a higher incidence of adjustment surgery both on the reconstructed breast and the opposite normal breast. Specifically, our findings were that such patients had a contralateral balancing surgery rate of more than 3 times that of patients with flap weights exceeding the mastectomy weights (37% versus 11% respectively) and a ratio of 37 to 1 with patients whose flap weights were equal to their mastectomy weight. Moreover, the same patient group (flap weight < mastectomy weight) had double the ipsilateral revision rate (17% vs 8% respectively) and almost three times that where the weights are the same (17% vs 6%). Interestingly, while there is a significant correlation between the rates of contralateral balancing surgery when the flap weight exceeds or is equal to the mastectomy weight (11% vs 1% respectively), the same is not true for ipsilateral revision surgery (8% vs 6% respectively) [Figure 3].

These sets of findings indicate that flaps should ideally be the same, where this is feasible, or heavier than the mastectomies in order to reduce the likelihood of future adjustment operations. The statistically significant increase in adjustment surgery when the flap:mastectomy ratio is less than one is an important finding and has implications for preoperative patient counselling and intraoperative flap trimming and contouring. Indeed, being aware of this factor makes it possible to adequately inform breast free flap patients before surgery that if they have an insufficient amount of abdominal tissue, they are more likely to need further adjustment surgeries. Notwithstanding this, making such patients aware of what they may face, might enable surgeons to at least opt for alternative reconstructive methods thereby potentially avoiding future adjustment surgeries. This is important from both the patient's perspective and in terms of reducing healthcare costs. However, this may be unavoidable if the patient insists on abdominal flap reconstruction and declines implant-based reconstruction. Such a scenario can be overcome by resorting to complex bipediced free flap reconstruction,<sup>24-27</sup> especially in those patients for whom adjuvant radiotherapy (RT) is planned.

It is not surprising that the patients whose flaps were lighter than the mastectomy weights had the highest incidence of adjustment surgery. This is because in order to achieve symmetry with the smaller reconstructed breast, a breast reduction or mastopexy was generally required. Similarly, when patients had RT, the radiation caused the index breast to fibrose and shrink and thus were more likely to need adjustment surgery in the form of flap scar revision. The effects of RT include causing scarring in the tissues and accentuating fibrosis in the irradiated tissues.<sup>28-30</sup> Therefore, this patient group had a significantly high incidence of flap scar revisions, which accounted for the higher ipsilateral adjustment surgery rate.

The present study has some limitations including the retrospective nature of the data collection. This led to some patients being excluded from the analysis. Furthermore, this study was not designed to elucidate the type of advisable adjustment surgery in the three respective groups nor whether the patients underwent RT. These aspects will be the subject of future investigations. On the other hand, this was a large multicentre study (n = 525 patients) with multiple surgeons as well as being international and therefore drawing on the experience of different healthcare systems. These factors combine to render the results more widely applicable.

## **CONCLUSIONS**

The present study demonstrated a flap-to-mastectomy weight ratio of less than 1 significantly increases subsequent adjustments on both contralateral and reconstructed breasts whilst irradiation disproportionately predisposes to ipsilateral revisions. These findings are important in patient counselling and intraoperative flap contouring. They may also play a role in planning subsequent aesthetic refinements. It is our recommendation that flap weight should ideally approximate or exceed mastectomy weight in immediate unilateral FFBR.



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