



Can patients with multiple breast cancers in the same breast avoid mastectomy by having multiple lumpectomies to achieve equivalent rates of local breast cancer recurrence? Response to the preliminary Alliance 11102 trial report

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36 To the Editors: Rosenkranz and colleagues report reassuringly high success rates for breast conserving
37 surgery (BCS) in women with multiple ipsilateral breast cancers (MIBC)¹. Surgical management of
38 MIBC can pose a dilemma when more sensitive imaging modalities detect additional tumor foci that are
39 potentially amenable to adaptive forms of BCS employing oncoplastic techniques². Interestingly, there
40 was minimal use of therapeutic mammoplasty amongst these patients, the majority of whom had two
41 tumors (96%) separated by at least 2cm with the largest focus measuring $\leq 15\text{mm}^1$. Despite this highly
42 selected group, more than 80% underwent standard BCS without tissue rearrangement and three-
43 quarters of all conservation patients achieved clear margins with a single operation¹. There is potential
44 for resection of larger T2 multicentric cancers in the Z11102 trial using more advanced oncoplastic
45 surgery such as level II mammoplasties¹⁻². Furthermore, larger tumors are more likely to require a boost
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dose and there are concerns about adverse effects from a double radiotherapy boost following BCS for MIBC^{2,3}. There is limited data from phantom studies on relative positioning and delivery of two separate boosts^{2,3}. Despite a median largest tumor size of 15mm, these patients received a boost to each tumor bed (10 - 16 Gy) that could lead to severe fibrosis with an estimated 10% increase in volume of breast tissue exposed to >60Gy³.

Although there is lack of high quality comparative data from randomised or prospective cohort studies, a degree of surgical equipoise exists which prompted the latest St Gallen consensus to endorse BCS for some cases of MIBC⁴. In a systematic review involving 24 retrospective studies, only 6 compared rates of loco-regional recurrence (LRR) for BCS versus mastectomy², with rates of LRR ranging from 2 – 23% after BCS. Formal meta-analysis showed homogeneity amongst studies with equivalent rates of LRR irrespective of surgical procedure [risk ratio 0.94; 95% CI 0.65 – 1.36]². This may have partly reflected a similar case selection bias with surgeons choosing BCS for low risk patients and mastectomy for higher risk cases. Such confounding would lead to inconclusive results in terms of safety and clinical outcomes of BCS compared with mastectomy for MIBC.

A survey of UK surgeons confirmed that 90% supported a randomised trial evaluating the efficacy of BCS compared with mastectomy (+/- reconstruction) for MIBC^{2,5}. The MIAMI trial will open as a preliminary study to assess whether a sufficient number of eligible patients (n=50) can be identified who will accept a randomized intervention over a 15 months period^{2,5}. This feasibility phase will inform the main trial that is powered using a 2% non-inferiority margin on a predicted 5-year LRR of 2.5% between BCS and mastectomy for all types of MIBC involving individual tumor foci up to 50mm^{2,5}.

The authors declare no competing interests

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