

Experts call for adequate tumor-free margins in breast cancer surgery to reduce recurrence and improve survival

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Surgeons should aim to remove at least a 1-mm width rim (margin) of healthy tissue around a breast tumor to reduce the risk of cancer

returning and improve breast cancer survival worldwide, suggests the largest analysis of the evidence to date published by *The BMJ* today.

The findings indicate that inadequate margin widths may result in higher risks of distant recurrence (cancer returning in a different part of the body) and breast cancer mortality, as well as increased local recurrence (cancer returning at the same site).

The researchers say current international guidelines need revision to account for these new findings.

After [surgery](#), a pathologist measures the shortest distance between the [tumor](#) and specimen edge to establish the width of the margin. The specimen is usually "inked" on the edges with a special pen, so the pathologist can clearly see the end of the tumor in relation to [healthy tissue](#).

Cancer guidelines suggest that avoiding a tumor that touches the margin of healthy tissue after breast cancer surgery reduces local recurrence, but no data exist for distant recurrence.

To address this knowledge gap, an international team of researchers searched for published studies reporting on patients undergoing breast conserving surgery for early-stage invasive breast cancer who were monitored for a minimum of five years.

A total of 68 observational studies published between 1980 and 2021 involving 112,140 patients with [breast cancer](#) (average age 56 years) were included in the analysis. The studies were designed differently, and were of varying quality, but the researchers were able to allow for that in their analysis.

Tumor specimens were categorized as tumor "on ink" at the margin

(involved), close margins (tumor less than 2 mm from the margin, but not at the margin), and negative margins (tumor 2 mm or more from the margin).

Across all studies, 9.4% of patients had involved (tumor on ink) margins and 17.8% had tumor on ink or a close margin. The rate of distant recurrence was 25.4% in patients with tumor on ink margins, 8.4% in patients with tumor on ink or close, and 7.4% in patients with negative margins.

Compared with negative margins, tumor on ink margins were associated with around a two-fold increased risk of distant recurrence and local recurrence.

Close margins were associated with a 38% increased risk of distant recurrence and a two-fold increased risk of local recurrence compared with negative margins, after adjusting for chemotherapy and radiotherapy treatment after surgery.

In five studies published since 2010, tumor on ink margins were associated with a 2.4-fold increased distant recurrence as were tumor on ink and close margins (1.4-fold increased risk) compared with negative margins.

Two studies reported on overall survival, comparing patients with tumor on ink versus not on ink margins. Tumors on ink margins were associated with a 61% increased rate of mortality, while positive or close margins versus wider (negative) margins were associated with 32% increased rates of mortality.

The researchers acknowledge that most of these data are from observational studies with low to moderate quality evidence, so a causal association between margin proximity and distant recurrence cannot be

proven.

Nevertheless, they say this study collates data from about four times the number of patients included in a similar 2014 analysis, and is also the first to consider the association between distant recurrence and overall survival with margins.

As such, they say, "A margin of no tumor on ink is inadequate and we recommend a minimum tumor free distance of 1 mm from the margin for either invasive disease or ductal carcinoma in situ to ensure optimum oncological outcomes."

Recognizing that wider margins require further surgery, they suggest that decisions about re-excision "should be the product of an informed discussion between clinicians and patients with full disclosure of the risks of increased distant recurrence associated with close margins."

Differences between the various international surgical guidelines on the best width for margin clearance should also be standardized with prevention of distant [recurrence](#) a primary aim, they add.

More information: Margin status and survival outcomes after breast cancer conservation surgery: prospectively registered systematic review and meta-analysis, *The BMJ* (2022). [DOI: 10.1136/bmj-2022-070346](https://doi.org/10.1136/bmj-2022-070346)

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