Cryosurgery for early breast cancers: abridged secondary publication

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KEY MESSAGES

1. After cryosurgery for early breast cancers, residual cancer is likely to occur at the periphery of the cryoablation site.
2. Careful preoperative planning and intra-operative monitoring are crucial to ensure complete cryoablation.

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Introduction

Breast cancer is a leading cause of cancer-related death in women. Increased awareness and improved imaging technology and screening have led to earlier cancer detection and improved survival rates.[1]

Surgical removal of breast cancer remains the gold standard of treatment. Endoscopic, robotic-assisted, or ablative surgery enables quicker postoperative recovery, shorter hospital stays, smaller wounds, and improved cosmetic outcomes. Techniques for minimally invasive percutaneous ablation include cryoablation, radiofrequency ablation, and laser ablation.[2]

Cryoablation is performed under local anaesthesia and is associated with minimal pain.[3] It can be an alternative to surgery for patients who are unsuitable for surgical treatment due to contraindications, particularly those with comorbidities that increase the risk of perioperative complications.

A previous study in Japan comprised the largest series of cryosurgery for early luminal breast cancers measuring ≤15 mm.[4] The present study aimed to evaluate the safety, feasibility, and efficacy of percutaneous cryoablation for luminal and non-luminal early breast cancers.

Methods

Patients with biopsy-proven T1 breast cancers or ductal carcinoma in situ were screened for eligibility for cryosurgery. Those with solitary T1 breast cancers of any immunohistotype, with a tumour-to-skin surface distance >5 mm, were included. Patients with invasive lobular carcinoma or lobular carcinoma in situ, pregnancy or lactation, or retroareolar tumours were excluded. Eligible patients received counselling regarding treatment options: cryosurgery followed by standard breast-conserving surgery or conventional surgical treatment with or without axillary surgery. Patients who opted for cryosurgery were recruited.

Pre-cryoblation magnetic resonance imaging of the breasts was performed to exclude multicentric tumours and to accurately estimate tumour size. Positron emission tomography–computed tomography was performed to corroborate the findings. Patients with multifocal or multicentric tumours, or tumour size >2 cm, were excluded. All images were reviewed by a radiologist and a nuclear medicine physician.

Cryosurgery was performed using the IceCure ProSense Cryoablation System. Preoperative ultrasound was used to localise the index tumour. The cryoprobe was inserted through the epicentre of the tumour; cryosurgery was performed according to the protocol. Intra-operative monitoring of ice-ball formation was undertaken. Cryosurgery was considered complete when a circumferential margin of 14 mm was achieved. Axillary surgery (such as sentinel node biopsy or axillary dissection) was performed where appropriate.

Post-cryoablation imaging was performed at 6 weeks. Lumpectomy of the cryoablated tumour was performed at 8 weeks. Intra-operative ultrasound was used to assess the cryoablated tumour, and a circumferential margin of at least 1 cm was excised for histopathological assessment. Specimens were sent for evaluation of cryoablation completeness. The primary endpoint was the complete ablation rate (%); secondary endpoints included risk factors for incomplete ablation and complication rates (%).

Results

Of 22 patients recruited, seven were excluded due to tumour size >20 mm. The remaining 15 patients underwent cryosurgery under general anaesthesia followed by lumpectomy and breast-conserving surgery. Their median age was 53 (range, 40-67) years. Five patients had ductal carcinoma in situ,

whereas 10 patients had invasive ductal carcinoma (IDC). Among the latter, five had luminal-type cancers (three luminal A and two luminal B), three had HER2-enriched invasive carcinoma, and two had triple-negative IDC. The 10 patients with IDC also underwent sentinel node biopsy. None had clinical or radiological nodal metastases. Median tumour sizes (largest dimension) were 13 mm (range, 8.6-18 mm) on ultrasound and 16 mm (range, 10-20 mm) on magnetic resonance imaging; ultrasound slightly underestimated tumour size.

The median cryoablation time (freeze-thaw cycle) was 75 (range, 25-101) minutes. Ten patients received two cycles to achieve the desired ice-ball size, whereas five patients received ≥3 cycles. The median ice-ball size was 44.5×44.5×45.2 (range, 35×37×36 to 58.5×60×60) mm.

In the lumpectomy specimen, seven patients had residual cancer: six with residual IDC and one with residual ductal carcinoma in situ. All residual cancers were identified at the periphery of cryoablated breast tissue. Ischaemic necrosis and fat necrosis were observed in other areas. Cell viability and immunohistochemistry tests did not reveal viable cancer cells at the centre of the cryoablated tumour in any of the 15 patients.

Among the seven patients with residual cancer, six had IDC: triple-negative IDC (n=1), HER2-enriched IDC (n=1), and luminal cancers (n=4). Among the six patients with IDC, three had a Ki-67 index ≥18%; tumour sizes were ≤15 mm in four and >15 mm in two. Among the seven patients with residual cancer, the median three-dimensional sonographic tumour size was 13.5×13.7×12.7 (range, 10.5×9.3×6.6 to 14×12.6×15) mm. Among the eight patients without residual cancer, the median sonographic tumour size was 11×11.6×9.5 (range, 11.2×8×8.6 to 17.5×16.4×17.1) mm.

Residual cancer after cryoablation was not associated with histotype, tumour size, Ki-67 index, ice-ball size, procedure duration, or number of cryosurgery cycles. All tumours were completely ablated centrally. No patients developed postoperative complications such as frost injury, bleeding, or haematoma.

Discussion

Cryosurgery is effective in treating small (≤15 mm) luminal-type breast cancers.[4] Cryoablation is achieved through freeze-thaw cycles, leading to tumour cell death and destruction of the vasculature. The initial results of cryosurgery at our institution were less than satisfactory, with a residual cancer rate of up to 46.7%, reflecting a steep learning curve.

None of the tumour- or surgery-related factors was associated with an increased risk of residual cancer after cryoablation. There was a trend towards a higher residual cancer rate in tumours >15 mm than in tumours ≤15 mm (42.9% vs 12.5%); however, this difference did not reach statistical significance, likely due to the small sample size. The three-dimensional size of the tumour should be considered.

Our findings suggest the presence of a learning curve for cryosurgery. Appropriate pre-treatment surgical planning is vital. The operating surgeon should fully understand the orientation of the tumour and its relationship to ice-ball formation, which is oval rather than spherical. It is crucial that the cryoprobe is inserted along the long axis of the tumour. Estimation of the number of freezing cycles required is fundamental to successful cryosurgery. The ice-ball must be sufficiently large to encompass the entire tumour with an adequate margin.

Conclusion

Given the higher residual cancer rate in tumours >15 mm, cryosurgery for these tumours is not recommended. Cryosurgery may potentially be applied to breast cancer types other than luminal breast cancer.

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Disclosure

The results of this research have been previously published in:

1. Kwong A, Co M, Fukuma E. Prospective clinical trial on expanding indications for cryosurgery for early breast cancers. Clin Breast Cancer 2023;23:363-8.

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