IntraOperative Cryoablation Therapy (IOCT): A Novel Alternative to Post-Lumpectomy Radiation Therapy

James V. Pellicane, MD, FACS[1], **Darius Francescatti**, MD, JD, FACS[2], **John M. Baust**, PhD[3], **Sean Caroll**, PE, MBA[4], **Diana Tucker**, BS, MBA[5]

National Consortium of Breast Centers

U.S. National Science Foundation

BACKGROUND

The incidence of breast cancer continues to rise, particularly in US women under the age of 40.[1] These women are in the prime of their lives with an estimated 40 more years to live.[2] Many are mothers, still of child-bearing age, and solidifying their professional careers. Today, breast cancer patients have two choices for treatment of their breast cancer: 1) surgical excision of the cancer followed by radiation therapy or 2) removal of the cancerous breast (mastectomy).[3]

Radiation treatment nonadherence is common among breast cancer patients due to its toxic effects and impact on quality of life.[4,5] Common complaints include fatigue, skin damage and required extended time off work. These effects are cataloged extensively on social media.[6] A survey of 26 US women with early-stage breast cancer revealed that 88% of respondents would prefer a non-radiation alternative to standard radiation therapy. Furthermore, 96% of respondents indicated they would pay out-of-pocket expenses for an alternative to radiation therapy.[7]

Non-adherence to radiation treatment increases the patients' risk of recurrence and potential mortality.[4] Non-radiation alternatives can eliminate this critical treatment gap. If an FDA-approved alternative to radiation therapy was available, breast surgeons and oncologists would consider non-radiation therapy for select patients with breast cancer [survey of 29 surgeons, oncologists, and pathologists].[7] In the same survey, 100% of hospitals that currently were unable to offer a breast cancer program would be able, and desire, to open one that did not require radiation.

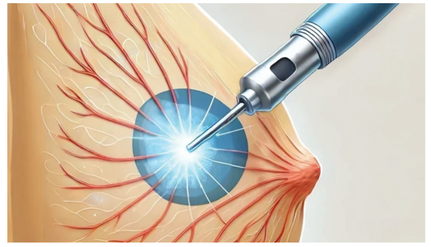

Figure 1. Rendering of SenoGuard IOCT targeting breast cancer cells.

SenoGuard is developing an intraoperative cryoablative therapy (IOCT) device that would be administered by the surgeon as an essential element of breast-conserving surgery **(Figure 1)**. This offers a potential third treatment option that could eliminate the need for radiation. Unlike small solid tumor cryoablation, which is done percutaneously and is only effective for tumors less than 1.5 cm, IOCT can be used to reduce the likelihood of local tumor recurrence by targeting the tumor bed after excision for any residual cancer, similar to IORT.

In this proof-of-concept study that was funded by the National Science Foundation (NSF) in 2023 [#2208433], we aimed to evaluate the feasibility and safety of cryoablation of the surgical cavity using a new 2 cm cryoablation probe and cryogenic system as a potential alternative to radiation therapy. A second NSF grant was awarded in 2024 [#2404500] to test the final design prototype in-vivo for FDA submission.

METHODS

An excision was made within the breast tissue of a porcine ex vivo tissue model to simulate the technique used for tumor lumpectomy **(Figure 2)**. A probe delivering a novel nitrogen-based cryogen was inserted into the surgical cavity to cryoablate the surrounding cavity. Data on the delivery of specific isotherms at various depths and time points within the surgical cavity was collected using a thermocouple mandrel sensor to assess the technique's precision and efficacy. Separate studies using a 2 cm cylindrical and coiled cryoprobe were conducted.

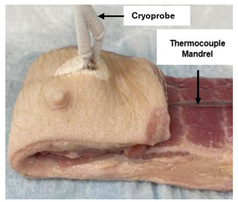

Figure 2. A representative experimental setup illustrating the positioning of the cryoprobe and thermocouple mandrel sensor in an ex vivo porcine breast tissue model.

RESULTS

Isotherm Profiles During 5.5-min Freezing Cycle

The study found that the cryoprobe was able to deliver -20°C isotherm to a depth of 1 cm from the cryoprobe surface following a 3-minute freeze cycle, demonstrating the potential for effective tissue cell destruction within this range **(Figure 3)**. These results were consistent with evidence from other cryoablation studies in breast cancer models.[8,9]

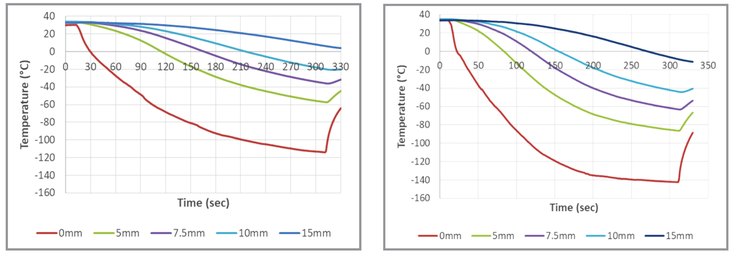

Figure 3. Real-time monitoring of the isotherm profiles generated by the (A) cylindrical and (B) coiled cryoprobe prototype at the center of the ablation segment during a 5.5-min freezing cycle.

Radius (mm) from the probe surface of given temperatures						
Freeze Duration		0°C	-10°C	-20°C	-30°C	-40°C
3 min	Average	8.6	7.3	6.1	5.2	4.4
	SD	0.9	0.9	0.9	0.9	0.8
5 min	Average	12.7	11.1	9.5	8.1	6.9
	SD	0.5	0.7	0.8	0.9	0.9
10 min	Average	16.7*	15.0	13.3	11.6	9.9
	SD	0.3	0.2	0.2	0.3	0.4

Table 1. Radius of the critical isotherms from the surface of the cylindrical cryoprobe in the ex vivo porcine breast tissue.

Radius (mm) from the probe surface of given temperatures						
Freeze Duration		0°C	-10°C	-20°C	-30°C	-40°C
3 min	Average	12.5	11.2	10.0	8.9	7.9
	Standard Deviation	0.6	0.7	0.8	0.8	0.9
5 min	Average	15.7*	14.7	13.6	12.5	11.4
	Standard Deviation	0.6	0.6	0.7	0.8	0.9

Table 2. Radius of the critical isotherms from the surface of the coiled cryoprobe in the ex vivo porcine breast tissue.

Delivery of Critical Isotherms at Various Temperatures

Extending the freeze cycle to 5 minutes resulted in delivery of the 40°C isotherm to reach a depth of 1 cm, indicating a more intense and potentially more effective treatment for slightly larger tumor cavities **(Tables 1 and 2)**. Since the 0˚C isotherm had grown beyond the 15 mm thermocouple position at the end of the extended freeze, the data was extrapolated based on the temperature regression between the 10 mm and the 15 mm thermocouple positions.

CONCLUSIONS

Data from this feasibility study demonstrates that intraoperative cryoablative therapy could achieve similar results as created by radiation therapy. The ability to adjust freeze cycle duration based on tumor cavity size will allow for various sizes of tumors to be treated and may eliminate the need for post-lumpectomy radiation therapy in certain patient candidates. Additionally, advantages over traditional radiation therapy include potentially improved cosmetic outcomes, a lower risk of side effects, and greater accessibility and affordability for all patients.

Future Directions

SenoGuard IOCT could help countless women avoid the challenges of traditional radiation as well as provide cost-effective, state-of-the-art local therapy to underserved populations globally. Supported by two National Science Foundation grants, SenoGuard is poised to complete the human trials for FDA submission in the near future.

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Author Affiliations

1 Director, Breast Oncology, Bon Secours Virginia Health System, Virginia Breast Cancer Center, Midlothian, Virginia, USA
2 Adjunctive Assistant Professor of Surgery, Rush University Medical Center, Chicago, Illinois, USA
3 CEO and Lead Scientist, CPSI Biotech, Owego, New York, USA
4 Principal Investigator, SenoGuard, Orange County, California, USA
5 CEO of SenoGuard, Inc., Orange County, California, USA

Please feel free to contact diana@senoguard.com for more information

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