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Patient-Controlled Carbon Dioxide Tissue Expansion for Breast Reconstruction



Image courtesy AirXpanders Inc.

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Summary

- Women who choose breast reconstruction after a mastectomy may need tissue expansion to stretch the skin and muscle of the chest to accommodate the breast implant.
- Current saline-based tissue expanders require patients to visit health care providers multiple times over a period of months to receive saline injections.
- The AeroForm Tissue Expander System uses carbon dioxide to achieve tissue expansion. Women can self-administer the carbon dioxide at home, which may offer greater convenience and reduce the number of office visits needed.
- The AeroForm Tissue Expander System is currently marketed in Australia and the US, but not in Canada.
- Evidence on the AeroForm Tissue Expander System comes from one multi-centre, randomized controlled trial in the US, and from several small, single-centre, uncontrolled studies in Australia.

Background

After a mastectomy (surgical removal of the breast to treat or prevent breast cancer), some women choose to have breast reconstruction, either with prosthetic breast implants or autologous tissue (tissue from a patient's abdomen, thighs, or buttocks).¹ Post-mastectomy breast reconstruction helps improve quality of life and psychological well-being for many women, for example in terms of body image, self-esteem, and sexuality.¹⁻³

Breast reconstruction may be done at the time of the mastectomy or can be delayed as necessary. In either situation, tissue expansion over a period of months may be needed to mechanically stretch the skin and muscles of the chest to accommodate the breast implant.^{1,4-6} Currently, tissue expansion is achieved using saline injections into an implanted tissue expander device. The injections are administered by a trained health care provider (physician, nurse, or physician assistant) over several weeks or months following mastectomy.¹ When the expansion is complete, the tissue expander is removed and replaced (exchanged) with the breast implant.¹

A new device, the AeroForm Tissue Expander system (AirXpanders, Inc., Palo Alto, California) uses carbon dioxide gas to expand the tissue. This allows women to control tissue expansion themselves — without the need for injections or frequent physician office visits.⁵ The device may also reduce the time needed for tissue expansion, so women can receive their implants and return to their normal lives more quickly.⁵

The Technology

The AeroForm Tissue Expander System is a temporarily implanted device that includes a stainless steel container of compressed carbon dioxide.^{7,8} The carbon dioxide is released into a silicon-covered expander compartment using a wireless, patient-activated remote control.^{7,9} The expander implants are available in three sizes (small, medium, and large).^{8,9} Tissue expansion begins once the implantation site is sufficiently healed.⁶ The remote control is programmed to release a specific dose of carbon dioxide in increments of 10 cc per dose, with a maximum of one dose per three-hour period and up to three doses per day.⁵ The controller also tracks the dosing activity and volume of the expander.¹⁰ The physician can override the program and administer additional doses as needed.^{5,10} Once the planned expansion volume is reached, a maintenance dose is given until the breast is reconstructed, at which time the device is surgically removed and replaced with a breast implant.^{4,6} The device should not be implanted for more than six months.⁸

Availability

The AeroForm Tissue Expander system is not currently licensed by Health Canada.

In the US, the AeroForm system received FDA approval in December 2016 as a Class II device.^{11,12} The FDA approval states that the system is intended for women who have undergone



The AeroForm Tissue Expander System. Image courtesy AirXpanders Inc.

a mastectomy to expand the soft tissue to allow for breast reconstruction, and that it is also intended for “the treatment of underdeveloped breasts and soft tissue deformities.”^{11,12}

In Australia, where early studies of the device were done, the Therapeutic Goods Administration licensed AeroForm as a Class III device in 2013.¹⁰

Cost

Canadian cost information for the AeroForm Tissue Expander System is not available.

In Australia, the AeroForm system is reimbursed as a prostheses through national health insurance for AUD\$2,450 per expander.¹³ Bilateral breast reconstruction requires two AeroForm devices, each with a separate controller. (In future, it may be possible to use a single controller.)^{5,6}

Patient Group

Each year, approximately 22,000 Canadian women undergo mastectomy or breast-conserving surgery (lumpectomy).¹⁴ Mastectomy is mainly used to treat breast cancer, but some women at high risk for developing breast cancer may also choose to have a preventive mastectomy.^{3,6,14,15}

Not all women who have a mastectomy will have breast reconstruction. The procedure is generally an option for women with less advanced stages of cancer.² It is also more likely to be chosen by younger women, women with higher income levels, white and non-immigrant women, and women living in urban areas.² The main reasons women choose not to have breast reconstruction are the desire to avoid further surgery and lack of awareness about their options.¹

The AeroForm system is intended for women who have had a mastectomy and want to have breast reconstruction with a saline- or silicone-filled breast implant.⁸ Tissue expansion is generally not used when women have an autologous tissue implant or for women who need post-mastectomy radiation therapy.^{1,4}

Current Practice

Guidelines from Alberta and from the American Society of Plastic Surgeons recommend that women be informed of their options for breast reconstruction and offered a consultation with a plastic surgeon.^{3,16}

Most women who choose breast reconstruction receive tissue expansion using saline injections administered by a health care provider weekly or biweekly until breast reconstruction is complete.^{5,16}

Alternatives to breast reconstruction include using an external breast prostheses or no intervention.¹⁷

The Evidence

We found one multi-centre, randomized controlled trial with two published reports of preliminary results;^{5,7,15} three single-centre, non-randomized, single-arm prospective studies;^{6,17,18} and one case series⁹ evaluating the AeroForm Tissue Expansion System.

“Carbon dioxide-based tissue expanders carry risks similar to those associated with saline expander devices...”

XPAND Trial(US, 2016)^{5,7,15}

The XPAND trial was a randomized controlled trial funded by AirXpanders Inc. that compared the use of the AeroForm system with saline tissue expanders.⁵ The trial included 150 women between the ages of 18 and 70 at 17 US hospitals. A total of 168 AeroForm tissue expanders (98 women) and 88 saline tissue expanders (52 women) were implanted. The trial excluded current smokers and women with comorbidities, such as diabetes or obesity, or fibrosis from previous radiation therapy.⁵

Women who received AeroForm expanders were trained on how to use the devices and controlled the tissue expansion themselves, but their physicians saw them weekly during the tissue expansion phase to monitor their progress. Women who received saline expanders had saline injections administered by their physicians (frequency of injections not specified).⁵ Both the AeroForm and the saline expanders were implanted using similar surgical procedures. The use of acellular dermal matrix (soft tissue grafts) was similar in both groups.⁵

A second US study, XPAND II (involving approximately 60 women), was expected to be completed in March 2017.¹⁹

ASPIRE (2015)⁶

ASPIRE was a non-randomized, single-centre study of the AeroForm system conducted in Australia without a control group.⁶ Twenty-one women received AeroForm tissue expanders in procedures performed by the same physician. Thirteen women (68%) had undergone a bilateral mastectomy. A total of 34 AeroForm expanders were implanted using two different surgical approaches.⁶ Some of the women received the Aeroform implant at the time of their mastectomy, while others received it later.⁶

PACE Studies (Australia, 2014 and 2011)^{17,18}

The PACE 1 and PACE 2 studies were single-centre, manufacturer-funded, non-randomized studies conducted in Australia without a control group.^{17,18} The PACE 1 study was a feasibility study in seven women who received a total of 10 AeroForm tissue expanders.¹⁸ The study excluded women with comorbidities, such as those deemed to be at high risk for surgical or other complications, obese women, women who had previously had radiation treatment, and women who were current smokers.¹⁸

The PACE 2 study included 33 women who received a total of 61 AeroForm tissue expanders.¹⁷ Twenty-eight of the women had bilateral tissue expander implants.

The same physician performed all implantation procedures in the ASPIRE and PACE studies.

Australian Case Series

Another Australian study reported results in a small case series of 10 women who received a total of 14 AeroForm tissue expanders.⁹

Outcomes

Successful Expansion and Breast Implantation

The primary outcome of the XPAND trial was successful tissue expansion and breast implantation.⁵ One-hundred forty-nine (89.8%) of 166 tissue expanders were successfully exchanged with breast implants in the AeroForm group, compared with 82 of 88 (93.2%) successful exchanges in the saline expander group.⁵ The investigators concluded that the AeroForm tissue expanders were not inferior to saline tissue expanders. Breast reconstruction failed in 17 breasts (10.2%) in the AeroForm group and in six breasts (6.8%) in the saline expander group.⁵ There were six device-related failures in the AeroForm group (3.6%) and one device-related failure in the saline expander group (1.1%).

In the ASPIRE study, 32 of 34 implantations (94%) achieved successful tissue expansion and breast reconstruction. In two women, infection and issues with wound healing required the AeroForm device to be removed, but later breast reconstruction was successful.⁶

Time to Expansion and Reconstruction Times

In the XPAND trial, the median time to desired expansion was 21 days for 142 breasts for which data were reported in the AeroForm group compared with 46 days for 82 breasts in

the saline expander group.⁵ The time from tissue expander implantation to final breast reconstruction was a median of 108 days (142 breasts) in the AeroForm group, and 136 days (82 breasts) in the saline expander group.⁵

In the ASPIRE study, the average time to complete expansion with the AeroForm tissue expander was 22 days; the average time to complete breast reconstruction was 96 days.⁶

The seven participants who received the AeroForm tissue expander in the PACE 1 study had an average active expansion time of 15 days.¹⁸ In the PACE 2 study, the average time to full expansion in the 33 participants was 17 days; all expanders were successfully exchanged for breast implants.¹⁷ In PACE 2, the average time until breast reconstruction was 90 days.¹⁷

In the Australian case series report the average time to full expansion was 16 days.⁹ Four of the women needed their physicians to administer additional doses of carbon dioxide at follow-up appointments.⁹

Pain

The XPAND trial reported pain data when carbon dioxide-based tissue expansion began and again one week later.⁵ The average pain score was two on a scale of 10; no difference was noted between scores when tissue expansion was under way.⁵ Breast-related procedural pain was reported for 10 breasts in the AeroForm group (5.9%) and 10 breasts in the saline expansion group (11.4%).⁵

In the ASPIRE study, one woman reported significant breast pain.⁶ Breast pain was also reported by seven women in the PACE 2 study.¹⁷

Satisfaction With the AeroForm System

In the XPAND trial, 98% of patients and 90% of physicians rated the AeroForm system's ease of use as high (number of patients and physicians not reported).⁵ Seventy-eight per cent of participants (number of patients not reported) were satisfied with any version of the AeroForm system.⁵ Patient satisfaction with the modified AeroForm device used later in the study was 84%. Patient satisfaction with saline expanders was 91% (number of patients not reported).⁵

In preliminary results from the XPAND trial, the study authors reported that aesthetic results were "excellent and comparable to saline-based expansion," but details of how this was measured were not provided.¹⁵

The ASPIRE study reported that of the 19 participants who responded to a questionnaire after the procedure, 16 (84%) were very satisfied with their outcomes, and all found the AeroForm system convenient to use.⁶ In the PACE 1 study, all seven participants reported satisfaction with the results and said the AeroForm system was easy to use.¹⁸ In the PACE 2 study, 31 of 32 participants who responded to a survey questionnaire reported that the controller was "very easy to use," and one reported that it was "moderately easy to use."¹⁷ Regarding satisfaction with results of the expansion, 26 women (81%) reported being "very satisfied," four women (13%) were "moderately satisfied," and two women (6%) were "satisfied."¹⁷

Safety

Saline injections for tissue expansion are associated with patient discomfort, a risk of puncturing the expander, and a risk of infection.^{5,9} Reports from conventional tissue expansion studies indicate that expander or implant failure may occur in up to 18% of women — mainly due to problems with wound healing, such as tissue necrosis, infection, or inadequate tissue perfusion in the mastectomy flaps (breast skin spared during skin-sparing mastectomy to be used for the reconstructive surgery).⁵ Breast cancer treatments (radiation and chemotherapy), smoking, and comorbidities (such as obesity, diabetes, or connective tissue disease) are associated with higher rates of complications with tissue expansion and breast implantation.^{1,5,16}

Carbon dioxide-based tissue expanders carry risks similar to those associated with saline expander devices, including infection, delayed wound healing, accumulation of fluid at the surgical site (seroma), implant extrusion, and stretch marks.¹⁵

The XPAND trial safety outcomes found that adverse event rates per participant were similar between the AeroForm group (98 women) and the saline expander group (52 women).⁵ About 63% of participants in each group experienced adverse events of any kind (63 women in the AeroForm group and 33 women in the saline expander group). Device-related adverse events occurred in 21 women (21.2%) in the AeroForm group and in 10 women (19.2%) in the saline expander group. Adverse events were reported for 43.8% of breasts (n = 74) in the AeroForm group and 39.8% of

breasts (n = 35) in the saline group, including post-operative wound complications, post-operative infections, seroma, procedural pain, and other events of equal frequency between groups.⁵

Device malfunctions with the AeroForm tissue expander were also reported. Deflation (both gradual and sudden) occurred in 34 expanders (20%); over-inflation due to obstruction of the valve releasing the carbon dioxide occurred in five expanders (3%); and loss of controller communication occurred with nine expanders (5%). No device ruptures were reported.⁵

The XPAND trial authors noted that the rate of device-related adverse events decreased in the latter part of the trial after improvements were made to the AeroForm expander device, such as decreasing the expander size, strengthening the inner bag's durability, and adjustments to prevent valve malfunctioning.^{5,7}

The Australian case series of 10 women who received AeroForm expanders reported two complications (both seromas).⁹ In the ASPIRE study, two failed breast reconstructions occurred — one due to infection and another due to problems with wound healing — but neither was considered to be device-related.⁶ In both women, the expander was removed and subsequent revision surgeries were successful. The ASPIRE study reported infection in a total of six women; five cases were resolved with antibiotics and one required removal of the expander.⁶ Two women had breast seromas and 19 had back seromas associated with the surgical approaches used. These were resolved with needle aspiration.⁶

The PACE 2 study reported 25 adverse events that affected 19 of the participants.¹⁷ These included seven reports of breast pain, one breast hematoma, one infection, 10 reports of back seroma, and two reports of cellulitis.¹⁷ These and other adverse events were not considered to be device-related.¹⁷ The PACE 1 study reported two adverse events (delayed wound healing that resolved within a few weeks) in the seven participants.¹⁸ No infections or other serious adverse events or device-related adverse events were reported.¹⁸

Implementation Issues

Radiation Therapy

The safety of the AeroForm device in women who need to undergo radiotherapy was demonstrated with functional testing of 32 devices at radiation doses of up to 70 Gy.²⁰ Device components continued to function as intended.²⁰ In the XPAND

trial, two women received radiation therapy with the AeroForm expander in place.⁵ Radiation treatment and subsequent breast reconstruction were completed for both women.⁵

Similarly, in the ASPIRE study, three women underwent radiation therapy with the expander in place, and no adverse events were reported.⁶ However, it may be necessary to make changes in radiation therapy planning to accommodate the device.^{6,21} The manufacturer's instructions for use note that, when possible, radiotherapy should be avoided when the expander is in place.⁸

Chemotherapy may be administered with the expander implanted.⁵ However, magnetic resonance imaging is contraindicated because it may damage or displace the implants.^{8,9} Further contraindications are listed in the manufacturer's instructions for use.⁸

“The convenience of patient-controlled tissue expansion may particularly benefit women in remote areas...”

Reversal of Expansion

One possible drawback to the AeroForm expander is that, unlike saline expanders, expansion cannot be reversed other than by puncturing the expander with a needle, which requires its removal.^{15,18}

Air Travel

The AeroForm expander will temporarily expand with increased altitude; therefore, the carbon dioxide dose should be decreased in the weeks before air travel to allow for this expansion.^{5,6} Women with an expander implanted should not fly before the surgical incision is properly healed.¹⁷ Three women in the XPAND study, four women in the ASPIRE study, and two women in the second PACE study flew with the AeroForm device in place.^{5,6,17} These women noted a sensation of fullness, but no significant discomfort.^{5,6,17}

Training

Patients will need training in the use of the AeroForm Tissue Expansion System.¹⁷ Although women can administer the carbon dioxide doses themselves, they will still need physician oversight.⁶ Study reports mention weekly follow-up by the physician throughout the expansion period,^{6,17} then monthly until permanent breast implant surgery; it is not yet clear what this means in terms of frequency of office visits in clinical practice.

One study noted initial difficulties with determining the sizing of the planned breast implants due to permeation of the carbon dioxide in the expander (and reduced expansion as a result) before the exchange occurred.²² An early study noted the need for physicians to add volume beyond preset limits to maintain the level of expansion.¹⁷ Delays in final breast implantation – for example due to follow-up cancer treatments or complications – could also pose problems if they extend beyond the maximum six-month period allowed for AeroForm implantation.²²

Uptake

One marketing source estimated that 3,000 tissue expanders may be sold in Australia each year. (Australia’s population is just over 23 million.)²³

The convenience of patient-controlled tissue expansion may particularly benefit women in remote areas who would otherwise need to travel frequently to receive saline injections over a period of months.⁹

Cost-Effectiveness

Overall treatment costs, including out-of-pocket and opportunity costs to patients, may be reduced due to the need for fewer physician office visits,¹⁵ but we found no published cost analyses to support this potential benefit.

Barriers to Breast Reconstruction in Canada

Far fewer Canadian women undergo breast reconstruction compared with women in the US and elsewhere.^{2,3,14,24} In one Ontario study, an estimated 16% of women who had a mastectomy underwent immediate breast reconstruction compared with about 38% of women in the US during the same period.¹⁴ Lower use of breast reconstruction in Canada may be due to less access to plastic surgeons as well as to other barriers, such as access to operating room time.^{2,25} In addition, national legislation in the US requires insurers to cover the costs of post-mastectomy breast reconstruction.^{1,24,26}

A 2011 Canadian study found that a variety of factors contribute to the relatively low use of breast reconstruction here: women’s lack of awareness about their options, long wait times, economic and cultural differences, living in rural or remote areas, physician knowledge and attitudes, and lack of Canadian guidelines on breast reconstruction.²⁴

Final Remarks

Although the AeroForm tissue expander has been available in Australia for several years, there is still limited evidence on the technology. An Australian commentary suggested that the AeroForm system should be included in the Australian Breast Device Registry to collect long-term data and allow independent assessment of its value.²⁷ In addition, study participants to date have been highly selected; therefore, the results may not apply to a broader patient population.²²

Methods – Literature Search Strategy

A peer-reviewed literature search was conducted using the following bibliographic databases: MEDLINE, PubMed, Embase, and the Cochrane Library. Grey literature was identified by searching relevant sections of the *Grey Matters* checklist (<https://www.cadth.ca/grey-matters>). No methodological filters were applied. The search was limited to English-language documents published between January 1, 2011 and December 14, 2016. Regular alerts updated the search until project completion; only citations retrieved before May 3, 2017 were incorporated into the analysis. Conference abstracts were not excluded from the search results.

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