CairnSurgical:
Patient-Specific, Real-Time Guidance for Breast Cancer Surgery

Breast-conserving lumpectomy followed by radiation is becoming a popular and equally efficacious alternative to mastectomy for the treatment of breast cancer. However, some 20-30% of the time, cancerous cells remain in the cavity around the excised tissue, a situation that calls for additional surgery. CairnSurgical aims to increase surgical precision with a custom guide that intraoperatively defines the contours of the tumor.

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Since the mid 80's, breast conserving surgery (lumpectomy) followed by radiation has become an efficacious option for the treatment of many breast cancers, and it's clearly a less traumatic option for women than having their entire breast removed. A lumpectomy is entirely successful when a surgeon achieves clean margins around the excised tissue, clean in this context meaning that the tissue on the surface of the specimen contains no cancer cells. This is somewhat challenging to accomplish, however, since surgeons are rarely guided by the kind of intraoperative imaging (MRI) that would allow them to see the tumor, although pre-operative MRI gives them a roadmap.

In the absence of real-time tissue imaging, various alternatives for localizing the tumor have been developed, starting with the most widely used method, wire localization. This involves a separate pre-operative procedure in the radiology department for insertion of a wire into the center of the tumor, under x-ray or ultrasound guidance, to point the surgeon to the tissue of interest. This is a potential source of delays and scheduling issues. Moreover, some 20-30% of the time, after the excised tumor is sent off for analysis, cancerous cells are detected in the margins. In that case, the patient must come back for a second surgery to remove the tissue, a situation that is frustrating to both patients and surgeons and costly.

To increase the odds of success, some surgeons sometimes shave off an additional millimeter around the tumor for good measure, but that doesn't guarantee clean margins either; surgeons are still operating blind and it's not a patient-specific strategy.

Between the US and Europe there are about 560,000 lumpectomies each year, and procedure volumes are growing because of better early breast cancer detection and reimbursement improvements. "It's a pervasive and persistent problem," notes David Danielsen, CEO of **CairnSurgical Inc.**, a start-up that's out to help surgeons remove breast cancer with more precision. CairnSurgical has invented a 3D printed shell with landmarks, which, created for a specific patient from her pre-operative MRI scan, can be simply placed on her breast during surgery for guidance.

Indeed, such a large and important medical problem has attracted many innovators but among them all, CairnSurgical offers perhaps the simplest solution, and one that takes into account that a tumor is three dimensional and often irregular in shape. The company is now in the process of confirming, clinically, that its solution is more successful than the standard of care.

Breast Cancer Comes in all Shapes and Sizes

As noted, intraoperative breast cancer localization is a fruitful area of innovation. Some strategies for dealing with this problem include the preoperative placement of seed-like implants that are radioactive, magnetic, or reflecting such that they can be found intraoperatively with various hand-held devices. **Merit Medical**'s *Scout Radar Localization*, for example, part of the company's recent acquisition of

Cianna Medical, uses non-radioactive implants. Another strategy involves the use of fluorescent markers that attach selectively to cancer cells, allowing them to be fluoresced and detected by special hand-held devices. (Such approaches are in the development pipelines of **Avelas Biosciences** and **Lumicell Inc.**) Widely used *MarginProbe* (developed by Dune Medical, which is now part of **Dilon Technologies Inc.**) is a device that uses radiofrequency electrical fields to see if there is any cancer in the margins of the excised tissue while the patient is still on the table, so a surgeon can remove more tissue if necessary, but it isn't guiding the surgeon during the first-pass excision procedure.

The challenge of removing an entire breast tumor with clean margins, especially while operating somewhat blindly (i.e., without intraoperative imaging) is compounded by the fact that a tumor isn't necessarily spherical and symmetrical like a golf ball; cancerous masses can be spherical, oval, or either of those shapes with lobes; irregular with projections; or spiculated, i.e., exhibiting linear projections from the margins. Most tumors aren't in fact spherical in shape, according to a study published in *Breast Cancer Research and Treatment* in July 2020, and that's perhaps why sticking a single wire into the center of a tumor fails to result in clean margins in almost a third of cases.

Furthermore, preoperative breast MRI is usually done with the woman in the prone position because it's easier to see the cancer that way. However, patients are supine when surgeons operate, so the shape and relative position of the tumor on the preoperative images doesn't match the surgeon's intraoperative view. "We see this as a three-dimensional problem that can't be solved with a mammogram or a single breast MRI of a woman who is facing down," says Danielsen.

At the instigation of surgeon Richard Barth Jr., MD, who is chief of general surgery at the Dartmouth-Hitchcock Medical Center, CairnSurgical was founded to find a better solution to the problem. He enlisted two Dartmouth engineers, Venkat Krishnaswamy, PhD, a former faculty member at the Thayer School of Engineering at Dartmouth, and Keith Paulsen, PhD, a professor of biomedical engineering at Thayer, who holds other distinguished positions at Dartmouth-Hitchcock, including scientific director of the center for surgical innovation and co-director of Translational Engineering in Cancer Research at the Norris Cotton Cancer Center.

As a first step, says Danielsen, they decided to do a supine MRI, "because that's the position the patient is going to be in when she gets her operation." From there, a few other ideas were iterated, before the company hit upon the winner, called the "*Breast Cancer Locator*," or *BCL*.

About two weeks before the surgery, the woman goes in for a preoperative MRI scan, which is customary, with the exception that in this case the views are taken from the supine position. The company takes the supine MRI data, analyzes it for the shape, size, and location of the tumor, then uses that to build a 3D printed plastic form designed for the patient's breast. It cups the breast and has landmarks that tell the surgeon how deep and how wide to go. The company then prints the *BCL* device and puts it in a kit with some wires and markers for shipment to the surgeon's office within 7-10 days.

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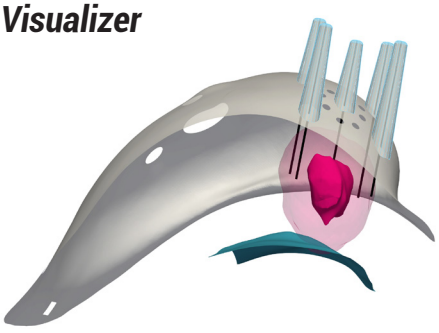
From the MRI data the company also creates an interactive *Visualizer*, a web-based program that depicts a 3D model of the tumor, which can be manipulated by the surgeon to show the shape of the tumor through the particular view, the dimensions, its location, and a darker boundary around the tumor that represents a 1 cm margin. The *Visualizer* also includes measurements of the distance from chest wall to the tumor and from skin surface to the tumor. The *Visualizer* can be used for pre-planning ahead of surgery and serves as a reference during the surgery itself (see *Figure 1*).

Figure 1

BCL and Position of the Tumor as Seen Through the _Visualizer_



Source: CairnSurgical

At the time of the procedure, the surgeon uses landmarks on the *BCL* to place it on the woman's breast accurately, uses ports on the device to insert wires into the breast as well as make marks on the surface of the breast outlining the shape of the tumor, then removes the device. One wire goes into the center of the tumor, as is done with the standard of care, but an additional four wires mark the tumor margins. Because this wire insertion is performed at the beginning of surgery when the patient is already anesthetized, there is no separate procedure needed and no associated pain, unlike traditional wire localization. The surgeon can also use a marker to mark the tumor's edges through open dots on the BCL. "In four to five minutes, the surgeon now has several important pieces of information," Danielsen says.

CairnSurgical has embarked upon a prospective randomized study, which will enroll 448 patients at a mix of 14 centers in the US—large academic, small rural, urban, specialized breast centers—designed to show that the *BCL*-aided surgeries result in superior outcomes to standard wire localization. The company is shooting to finish study enrollment late this year or early next year, according to Danielsen.

Danielsen notes that the study design is adaptive. "We can do interim analyses to see if we need to power up, or, for that matter, if we've already proven superiority, to stop." That approach could help the $12 million the company has raised so far go farther. The company has been funded through a Series A round led by the Morningside Group plus grants from the National Cancer Institute, the New Hampshire Innovation Research Center, and private investors.

In addition to clinical superiority, the company believes it can provide advantages from the health economics standpoint. "We are eliminating the radiology procedure, that's one cost that doesn't need to happen." In value-based scenarios or in economies that penalize repeat surgeries, the *BCL* could have additional advantages, if it proves to be more accurate than the standard of care and thereby avoids repeat surgeries. At the same time, companies introducing new products always need to prove that they aren't adding cost to an existing procedure. "We are confident that we can get it down to a cost and a price that actually reduces the hospital's cost," Danielsen says. MTS

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