

BREAST CANCER IN FOCUS

Current Developments in the Management of Breast Cancer

Section Editor: Hope S. Rugo, MD

Real-World Use of Scalp Cooling to Reduce Chemotherapy-Related Hair Loss



Hope S. Rugo, MD
 Professor of Medicine
 Director of Breast Oncology and Clinical Trials Education
 UCSF Helen Diller Family Comprehensive Cancer Center
 San Francisco, California

H&O How long has scalp cooling been in use as a method to reduce hair loss during chemotherapy?

HR Scalp cooling involves the use of cold caps on the head before, during, and after chemotherapy to constrict blood vessels in the scalp. The goal is to reduce the flow of chemotherapy to hair follicles in the scalp, interfering with the ability of chemotherapy to cause hair loss without impacting the effectiveness of treatment. Scalp cooling is also thought to reduce metabolism in the hair follicle cell, which in turn may help protect the cell from the toxic effects of chemotherapy.

Scalp cooling was introduced in the 1970s in Europe and Canada with a series of chilled caps that were changed during treatment. It was subsequently introduced in the United States, but this approach did not gain widespread use for several decades. First, the efficacy of the older manual caps was disappointing. Second, clinicians were concerned that scalp cooling might permit the local recurrence of cancer in the scalp. When clinicians in the United States became more interested in scalp cooling about a decade ago, 2 prospective trials were undertaken, resulting in the subsequent clearance by the US Food and Drug Administration (FDA) of 2 automated devices.

H&O What are the benefits to patients of reducing hair loss?

HR At least 80% of women with a diagnosis of early-stage breast cancer will be long-term survivors, and many

of these patients receive chemotherapy. Although we are now using chemotherapy in a more thoughtful manner than we once did, and fewer patients receive agents that will not help them, chemotherapy is still being administered in either the neoadjuvant or adjuvant setting to many patients with early-stage breast cancer.

The most common adjuvant chemotherapy regimens for early-stage breast cancer last for 3 to 5 months, although some last for 6 months. All these regimens lead to clinically

Losing hair can be a public declaration of what's going on—it's an obvious outward sign of illness.

significant or complete alopecia. Hair loss typically begins approximately 2 weeks after a chemotherapy regimen is started, or somewhat later with lower-dose weekly chemotherapy. Hair loss reaches its peak fairly soon thereafter.

The process of losing hair is traumatic, and the hair can take a year to grow back—or even more for women with long hair. Patients who receive certain chemotherapy regimens, particularly those that include docetaxel, can experience very slow hair regrowth. The hair may also be thinner when it grows back.

The effect of hair loss on patients can be substantial. Most women with a diagnosis of breast cancer are first of all interested in surviving their disease and not having a recurrence. But shortly thereafter, they become concerned about the toxicities of treatment. We can control many of those toxicities much better now than ever before, but effective treatments to prevent hair loss have lagged behind.

Many women will shave their head after the hair starts falling out, both to avoid having hair falling everywhere and because losing hair can cause scalp discomfort. Losing hair can be a public declaration of what's going on—it's an obvious outward sign of illness. Appearing ill may have ramifications for employment and personal relationships. For example, a woman who runs her own business may find that customers interact differently with her or doubt her ability to conduct business when they see her without hair. Hair loss also can be upsetting to the friends and family members of a woman who is undergoing chemotherapy. Some of my patients with young children wear a wig until their hair grows quite long to avoid that effect on their home life.

Of course, hair loss is less of an issue for some women. But for many women, it is a prominent issue in their daily life. Women can wear a wig, but these tend to be uncomfortable and hot—which is particularly bothersome for women who are experiencing hot flashes related to chemotherapy.

H&O Could you describe in detail the options that are available for scalp cooling?

HR There are 2 main types of devices used to prevent chemotherapy-induced alopecia—manual and automated (Table). The manual methods are older, but the manual methods that are now available can be quite effective. A gel-filled cap is chilled for at least 24 hours, placed on the head, and then covered by an insulating cap. The gel cap starts to warm as soon as it's placed on the head, so it is very cold at first and must be switched every 30 minutes. The use of gel caps requires that the chemotherapy center have either a freezer or a cooler filled with dry ice, along with thermometers to monitor temperature. Caps that have warmed also require special treatment; they need to be kept refrigerated to preserve the integrity of the gel. The caps are typically rented from a supplier, and a trained helper switches out the caps during treatment.

The FDA has approved 2 automated devices for scalp cooling. The DigniCap Scalp Cooling System from Dignitana was approved in December 2015 for use in women with breast cancer, and in July 2017 for use in patients with solid tumors. The Paxman Scalp Cooling System was approved in April 2017 for women with breast cancer.

The automated devices use a small machine on

Table. Scalp Cooling Systems

Manual
<ul style="list-style-type: none"> • Arctic Cold Caps (arcticcoldcaps.com) • Chemo Cold Caps (chemocoldcaps.com) • Penguin Cold Caps (penguincoldcaps.com) • Warrior Caps (warriorcaps.com) • Wishcaps (wishcaps.com)
Automated
<ul style="list-style-type: none"> • DigniCap Scalp Cooling System (dignicap.com) • Paxman Scalp Cooling System (paxmanscalpcooling.com)

wheels that can provide scalp cooling for 1 or 2 patients at a time. Coolant flows through a hose from the machine to a cap that looks like a swimming cap and comes in several sizes. The cap is cold, but not anywhere nearly as cold as the gel cap. It is covered by an insulating cap. The cap is used during the chemotherapy infusion as well as for approximately 30 to 45 minutes beforehand and an additional 20 to 150 minutes after the infusion ends.

When my group decided to study scalp cooling, we selected an automated device because it's easier for patients to keep the same cap on during the chemotherapy cycle than to have it changed every 30 minutes. The automated devices also maintain a more consistent temperature.

H&O Which major studies established the efficacy of scalp cooling?

HR There have been 2 large trials of automated scalp cooling in the United States, both of which were published in the *Journal of the American Medical Association* earlier this year. I was the lead investigator of the study using DigniCap, whereas Dr Julie Nangia of the Baylor College of Medicine in Houston, Texas, was the lead investigator of the study using the Paxman device.

Before embarking on our large trial, we conducted a pilot study together with Wake Forest Baptist Medical Center in Winston-Salem, North Carolina, that included 20 patients with stage I breast cancer who were scheduled to receive non-anthracycline-based adjuvant chemotherapy. We knew from previous studies that scalp cooling does not work as well in patients who receive anthracycline-based chemotherapy. After this study established the safety of the device, the FDA allowed us to proceed with our larger study of 122 patients at 5 sites with stage I or II breast cancer who were receiving non-anthracycline-based chemotherapy.

Our matched control group comprised 16 patients who did not want to use scalp cooling. Some people decline scalp cooling because they don't want to have do something extra during chemotherapy, dislike the idea of

being cold, or do not want to spend the extra time (up to 2 1/2 hours) after the chemotherapy for the postchemotherapy cooling. Although there were not cost issues with the study patients, some people will now decline standard clinical use because of cost. After we found that all the patients in the control group had complete hair loss, we halted enrollment in the control group per the agreement with the FDA.

At 1 month after the end of chemotherapy, we found that 66.3% of the patients who used scalp cooling kept at least half of their hair vs none of those who did not use scalp cooling.

In the study of the Paxman device, patients were randomly assigned in a 2:1 ratio to scalp cooling (119 patients) or a control arm (63 patients). Unlike the patients in our study, these patients were eligible even if they were receiving anthracycline-based chemotherapy. The study found that at interim analysis, 50.5% of the patients who used scalp cooling kept at least half of their hair vs none of those who did not use scalp cooling. There were no serious adverse events.

Knowing how to fit the cap is very important. The Paxman study included 7 sites, and analysis showed that the sites with the most experience in using scalp cooling tended to get the best results. For example, the site that enrolled just 1 patient for scalp cooling was unsuccessful with the device, whereas the site that enrolled 51 patients for scalp cooling had a 68.6% success rate.

H&O How many patients in the United States are receiving scalp cooling?

HR The number is increasing all the time. More chemotherapy treatment centers are purchasing and using the devices, so that clinicians and patients are becoming more convinced about the efficacy. Our center just installed a third device because the 2 devices we had were not adequate to meet our needs.

H&O What percentage of your patients with breast cancer are receiving scalp cooling?

HR I would say probably 60% of my patients with breast cancer use scalp cooling. Patients who receive a long course of paclitaxel followed by doxorubicin and cyclophosphamide are less likely to use it, although we are working to improve success rates in those patients. I think that this number will increase as technicians get better at cap fitting, more caps become available to fit patients with differently shaped heads, and experience with the devices increases. I expect that over time, we will see 70% or more of patients with breast cancer use scalp cooling.

H&O Are patients with other forms of cancer starting to use the cap at your institution?

HR Yes, we have seen a slow increase in use of the cap for patients with ovarian cancer, endometrial cancer, and other solid tumors that employ outpatient chemotherapy, resulting in significant alopecia. We also are using the caps in some men.

H&O How much does the treatment cost?

HR That depends on the geographic location and the number of treatments a patient receives. A typical amount is approximately \$1500, and a longer course of treatment might be closer to \$2500. Each institution must decide whether the patient will pay the scalp cooling device company directly and how much the institution will charge for cap fitting and placement. The machines are rented out by the companies and are serviced by their own service centers.

H&O Are insurers beginning to cover the cost of scalp cooling?

HR We have seen a few insurers provide some funding, but cost has been a real issue. Some philanthropic funding has become available for patients with the greatest financial need, but there is not enough funding for everyone. We are hopeful that insurance coverage will continue to expand.

H&O Are some clinicians resistant to using these devices?

HR There was a lot more resistance before these 2 studies came out. Now that the benefits have been proven, we have seen many more centers embrace the use of scalp cooling to improve supportive care. Scalp cooling is unlikely to be a money-making endeavor for centers, but I think patients will be more likely to choose centers where scalp cooling is available.

Another source of resistance to scalp cooling was concern about scalp metastases. However, that concern was not borne out by the 2 large studies, or by a meta-analysis recently published in *Breast Cancer Research and Treatment* of all reported safety data from prospective and retrospective trials. There's absolutely no evidence of an increase of scalp metastases in patients who receive scalp cooling.

H&O What are some of the disadvantages and side effects of the caps?

HR Gel caps can get very cold, so it is important that the staff receive instruction in their use to avoid thermal injury of the scalp. In 2016, a group at Memorial Sloan Kettering Cancer Center published a report on 4 cases of frostbite attributed to the use of cold caps. Another possible side effect is cold-induced eczema (flaking of the scalp). These problems seem to occur only with improper use of the gel devices, which are colder than the automated devices when first placed on the scalp. We have seen a single case of cold-induced eczema in patients using the automated devices; this resolves after the end of chemotherapy and cooling.

The most common side effect of cooling devices is headache, which makes sense because of the association between vasoconstriction and headaches. In our study, we found that 3.8% of patients experienced a mild headache. A few patients have reported a small increase in nausea, which I suspect may be related to either anxiety or a headache.

Having a cold cap on the head can make patients feel cold and uncomfortable overall, so we instruct them to use a warm blanket and sip hot tea when the cap is applied. The unpleasant feeling and “brain freeze” that some people experience generally happen during the initial cooling period. Once they’re cool, they’re okay. In our study, 2.8% of participants discontinued scalp cooling because they didn’t like feeling cold.

One limitation of the caps is that they can fail to come in contact with the head in certain spots. For example, a flat spot on the top or back of the head will not have good contact with the cap, and someone with such a spot may experience more hair loss there.

There are situations in which we do not recommend scalp cooling. For example, we would not expect it to be effective in someone undergoing inpatient intensive multiday chemotherapy for sarcoma.

H&O Do patients ask about scalp cooling, or are you usually the one who brings it up?

HR I think it’s fairly equal. When I explain the potential side effects of treatment to patients, including hair loss, I mention the option of scalp cooling. If the patient has any interest, our clinical coordinator provides more detailed information, including side effects, scheduling, and cost.

H&O What types of reactions have you received from patients who have used scalp cooling?

HR The feedback has been almost universally positive. Patients feel better about the way they look, and they

feel better overall about their experience because they’ve been able to control one aspect of their treatment. Even patients who lose a substantial amount of hair are pleased that they used the device, and many notice that their hair is growing back while chemotherapy is still under way.

We have shown that patients who used the Dignitana device had better scores on several quality-of-life indicators. We have also seen this in a registry study of the Penguin Cold Cap conducted at the University of California, San Francisco, and recently published in *Breast Cancer Research and Treatment*.

H&O Could you talk about the CHILL initiative?

HR Now that we have 2 large published studies and a huge resurgence of interest in scalp cooling, we want to gain a better understanding of how these devices work and which approaches work best with different chemotherapy regimens and different cancers.

The CHILL (Cancer-related Hair Loss, International Leadership and Linkage) initiative is an international registry intended to help clinicians better understand the effects of scalp cooling. It collects information from patients and physicians regarding clinical parameters, patient characteristics, and efficacy. It is supported by unrestricted grants from both Dignitana and Paxman.

Disclosure

Dr Rugo has received research support from Dignitana.

Suggested Readings

Alopecia and scalp cooling. Cancer-related hair loss, international leadership and linkage. www.scalpcooling.org. Accessed September 6, 2017.

Belum VR, de Barros Silva G, Laloni MT, et al. Cold thermal injury from cold caps used for the prevention of chemotherapy-induced alopecia. *Breast Cancer Res Treat*. 2016;157(2):395-400.

Nangia J, Wang T, Osborne C, et al. Effect of a scalp cooling device on alopecia in women undergoing chemotherapy for breast cancer: the SCALP randomized clinical trial. *JAMA*. 2017;317(6):596-605.

Rice BA, Ver Hoeve ES, DeLuca AN, et al. Registry study to assess hair loss prevention with the Penguin Cold Cap in breast cancer patients receiving chemotherapy [published online September 18, 2017]. *Breast Cancer Res Treat*. doi:10.1007/s10549-017-4506-z.

Rugo HS, Klein P, Melin SA, et al. Association between use of a scalp cooling device and alopecia after chemotherapy for breast cancer. *JAMA*. 2017;317(6):606-614.

Rugo HS, Melin SA, Voigt J. Scalp cooling with adjuvant/neoadjuvant chemotherapy for breast cancer and the risk of scalp metastases: systematic review and meta-analysis. *Breast Cancer Res Treat*. 2017;163(2):199-205.

Rugo HS, Serrurier KM, Melisko A, et al. Use of the DigniCap™ system to prevent hair loss in women receiving chemotherapy (CTX) for stage I breast cancer (BC). *Cancer Res*. 2012;72(24 suppl):A2.