# Safety and effectiveness of scalp cooling in cancer patients undergoing cytotoxic treatment

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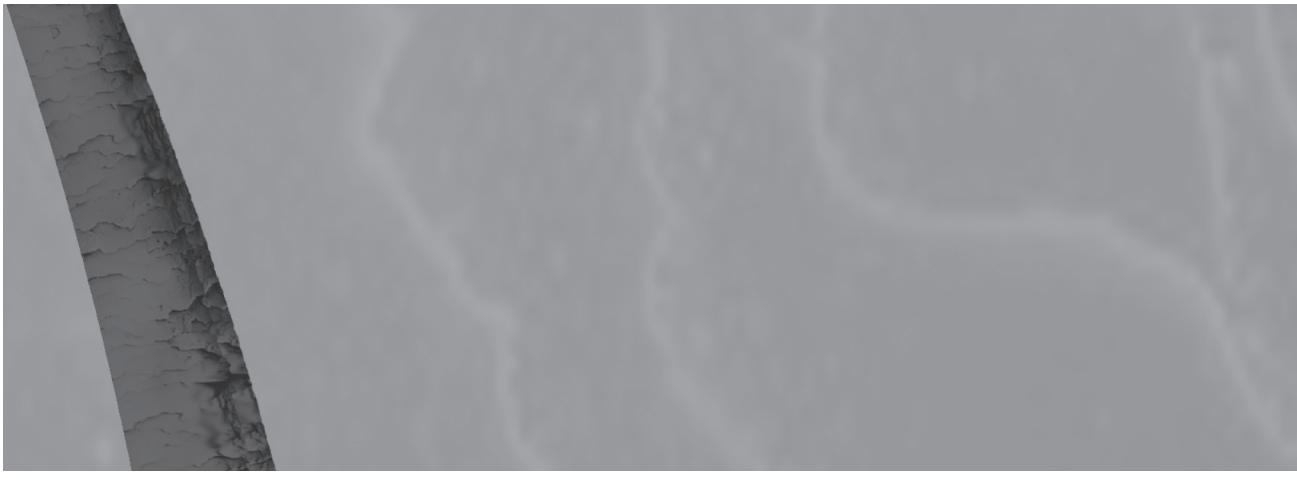
# Chapter 8



## Impact of alopecia and scalp cooling on the well-being of breast cancer patients

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## Abstract

### Objective

Chemotherapy-induced hair loss may be prevented by scalp cooling. This study focuses on the impact of chemotherapy-induced hair loss and the effect of scalp cooling on well-being.

### Methods

A prospective multi-centre study was performed in 13 hospitals. Breast cancer patients treated with (n=98) and without (n=168) scalp cooling completed questionnaires (EORTC QLQ-C30 and QLQ-BR23, WHOQOL-BREF, BIS, MBA, HADS) before chemotherapy, and three weeks and six months after chemotherapy.

### Results

Scalp cooling was effective in 52% of the cases. Hair loss was considered among the most distressing problems at all three moments of measurement. A trend towards higher well-being was found in successfully scalp-cooled patients, as indicated by a general better health related quality of life (HRQOL), better body image and a lower importance of hair for body image. Explanations for reduced well-being in unsuccessfully scalp-cooled patients might be disappointment due to hair loss despite scalp cooling or a higher biological availability of cytotoxics.

### Conclusions

Scalp cooling contributes to the well-being of successfully scalp-cooled patients, but also seems to cause additional distress when patients lose their hair despite scalp cooling. Therefore effort has to be undertaken to provide additional support to patients when scalp cooling is ineffective and to further improve the results of scalp cooling.

## Introduction

Hair plays a major role in our appearance and in our unique individuality: who we are is tied in varying degrees to how we look.[1] Hair is a symbol of identity and personality and there is an important link between hair and feelings of attractiveness, sexuality and femininity or masculinity.[1-3] Sudden severe hair loss is generally associated with illness. Alopecia, ranging from partly to total hair loss, is a common side effect of chemotherapy. Severe alopecia stigmatizes by changing the individual's identity from a healthy person into a cancer patient, for the person him- or herself, but also for others.[2,3] Therefore, it is not surprising that cancer patients frequently rate alopecia among the most severe, troublesome and distressing side effects of chemotherapy.[4-14]

Alopecia may seriously affect one's body image, which in turn has an impact on self-esteem and self-confidence.[15-17] Consequently, it may cause emotional suffering, may lead to personal, social and work related problems and may have an negative effect on quality of life.[1-3,18,19] However, the magnitude of the impact of alopecia might have been reduced since, first, nurses pay more and serious attention to the patients' coping with alopecia and, second, the possibilities for head covering have improved significantly in the past decades.

In an increasing number of countries, scalp cooling has been introduced to prevent or reduce chemotherapy-induced alopecia. Scalp cooling reduces toxicity of cytotoxics in the hair matrix cells and is applied in chemotherapy schedules that normally cause severe alopecia. However, the reported success rates of scalp cooling vary widely.[20]
Preservation of hair during chemotherapy is expected to contribute positively to the well-being of cancer patients. However, it is plausible that only those patients choose for scalp cooling who attach much value to their hair. If these specific patients loose their hair, despite scalp cooling, it is possible that they experience this as an additional burden. The current study focuses on the impact of chemotherapy-induced alopecia and the effect of scalp cooling on health related quality of life (HRQOL), body image, anxiety and depression in breast cancer patients.

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## Materials and methods

### Setting and Participants

Breast cancer patients were enrolled in this prospective multi-centre study between October 2004 and February 2007. Thirteen hospital locations participated, with six offering scalp cooling using the Paxman system. If patients in the scalp cooling hospitals did not choose for scalp cooling, they were not included in this study.

Specialised oncology nurses informed patients about the study. Patients who decided to participate, received a set of questionnaires (see measures section below) and return envelopes in the clinic and completed them at home. If questionnaires were not returned in time, the patient received a reminder.

Approval for this study was obtained from the Medical Ethics Committees of all participating hospitals.

## Inclusion and exclusion criteria

Inclusion criteria were having invasive breast cancer without distant metastases and signed informed consent. Moreover patients had to be treated with one of the following intravenous administered chemotherapies: 4 or 6 Adriamycine (60 mg/m²) and Cyclophosphamide (600 mg/m²) treatments (AC); 5 or 6 5-Fluorouracil (500 mg/m²), Epirubicine (90 mg/m²) and Cyclophosphamide (500 mg/m²) treatments (FEC); 5 or 6 5-Fluorouracil (500 mg/m²), Adriamycine (50 mg/m²) and Cyclophosphamide (500 mg/m²) treatments (FAC); and 5 or 6 Docetaxel (75 mg/m²), Adriamycine (50 mg/m²) and Cyclophosphamide (500 mg/m²) treatments (TAC). These schedules had to be administered in the adjuvant setting within a cycle of 21 days. Without scalp cooling these chemotherapies usually cause severe alopecia. Patients treated with intravenous trastuzumab for a year following chemotherapy were excluded of the third measurement because of the possible influence of long-lasting intensive contact with oncology nurses and other cancer patients on their answers on the questionnaires. Patients were also excluded if they lacked basic proficiency in Dutch, if they were unable to understand the patient information folder, or if they already suffered from alopecia before the onset of chemotherapy.

## Measures

### Patient and tumour characteristics

The measured patient and tumour characteristics were date of birth, marital status, educational level, type of surgery and lymph node dissection. Lymph node dissection includes sentinel node dissection as well as axillary lymphadectomy.

### Severity of alopecia

The success of scalp cooling was defined on the basis of whether the patient reported the use of a wig or head covering inside or outside the house. Patients additionally evaluated the severity of alopecia on the 4-point scale for alopecia of the World Health Organisation (WHO) with grade 0 for no alopecia, grade 1 for mild alopecia, grade 2 for pronounced alopecia and grade 3 for total alopecia.[21] Furthermore, patients filled in a Visual Analogue Scale (VAS) ranging from 0 (for no alopecia) to 100 (for total baldness).

### Impact of side effects of chemotherapy and consequences of cancer

Impact of side effects and consequences of cancer were measured by a so called 'psychophysical scaling method' that ranks physical and psychosocial disease and treatment effects that could possibly be experienced by breast cancer patients.[4] Patients rated the impact of each item, with alopecia serving as a reference value.[22] The following items were added to the original measure: arm problems, total mastectomy, breast changes, loss of appetite, change in taste, early hot flashes, and scalp cooling. Before the start of chemotherapy, this questionnaire assessed the patient's expectations regarding side effects and after chemotherapy it assessed the actually experienced side effects.

### Health related quality of life

HRQOL was measured by the European Organization for Research and Treatment of Cancer (EORTC) quality of life questionnaire (EORTC-QLQ-C30, version 3) and the EORTC breast cancer module (EORTC-QLQ-BR23).[23] These internationally validated questionnaires were

scored according to algorithms recommended by the EORTC, resulting in a 0 to 100 scale.[23,24] Higher scores represent better functioning or higher levels of symptoms.

### Body image

Body image was assessed with the revised version of the Body Image Scale (BIS, version 2).[25] Higher scores represent more symptoms or increased distress regarding body image.

Concern over body image was assessed by the Measure of Body Apperception (MBA).[26] The two subscales of this measure, labelled 'concern about appearance' and 'concern about body integrity', assess personal investment in body image, rather than assessing the body image the person currently holds, with higher scores mean more concerns.

Two self-defined items were added to measure the importance of hair for the respondent's body image. These items were 'my hair is important to me' and 'my hair is important for my appearance'. Response options were rated on a 5-point Likert scale ranging from 'strongly agree' to 'strongly disagree'. Higher scores mean higher importance of hair.

### Hospital Anxiety and Depression Scale (HADS)

The Dutch version of the HADS, which assesses anxiety (HADS-A) and depression (HADS-D),[27,28] was scored in the range from 0 to 21, with higher scores representing more distress.

### Time points

Patients reported the severity of alopecia three weeks after completing chemotherapy. All remaining questionnaires were completed before the onset of chemotherapy and three weeks after the last cycle of chemotherapy. Only the questionnaire on the impact of side effects and consequences of cancer was also measured six months after completing chemotherapy. These time points were chosen because after three weeks the final result of scalp cooling is known and after six months the hair has regrown to some extent.

## Statistical analyses



Statistical analyses were performed using SAS (version 9.1 for Windows, SAS institute Inc., Cary NC). Patient and tumour characteristics were compared between scalp-cooled patients and non scalp-cooled patients by a t-test for age and chi-square tests for categorical variables.

Data collected before the onset of chemotherapy were compared between patients who were about to have scalp cooling and those who were not. Three weeks and six months after having completed chemotherapy, scores of scalp-cooled patients who did or did not preserve their hair and patients who did not receive scalp cooling were compared. All group comparisons were made with analyses of variance followed by Tukey's test for multiple group comparison.

# Results

## Patient and tumour characteristics

In total, 98 scalp-cooled patients and 168 non scalp-cooled patients received the first questionnaire of whom 184 (68%) fully responded at all three measurements (Figure 1).

Dropout during the study occurred due to a variety of reasons, such as logistical problems in the administration and resending of the questionnaires, but also progression of disease (switch from adjuvant to palliative treatment), or additional treatment with trastuzumab. Patient and tumour characteristics of breast cancer patients treated with or without scalp cooling did not differ significantly between both patient groups (Table 1).

## Severity of alopecia

Three weeks after the last chemotherapy, data were available of 65% of scalp-cooled patients (n=64) and 89% of non scalp-cooled patients (n=149) (Figure 1). Scalp cooling was considered effective in terms of no need of head covering in 32 of 62 evaluable patients (52%). Two patients for whom information on alopecia was missing were excluded from further analyses. All but four non scalp-cooled patients who completed the second questionnaire (n=149) reported to wear a wig or head covering. These four patients were, however, completely bald and were excluded from further analyses, because of their low number.

The mean rating of alopecia on the VAS scale among successfully scalp-cooled patients was 49 (range 17 to 97) while not successfully scalp-cooled patients had a mean score of 79

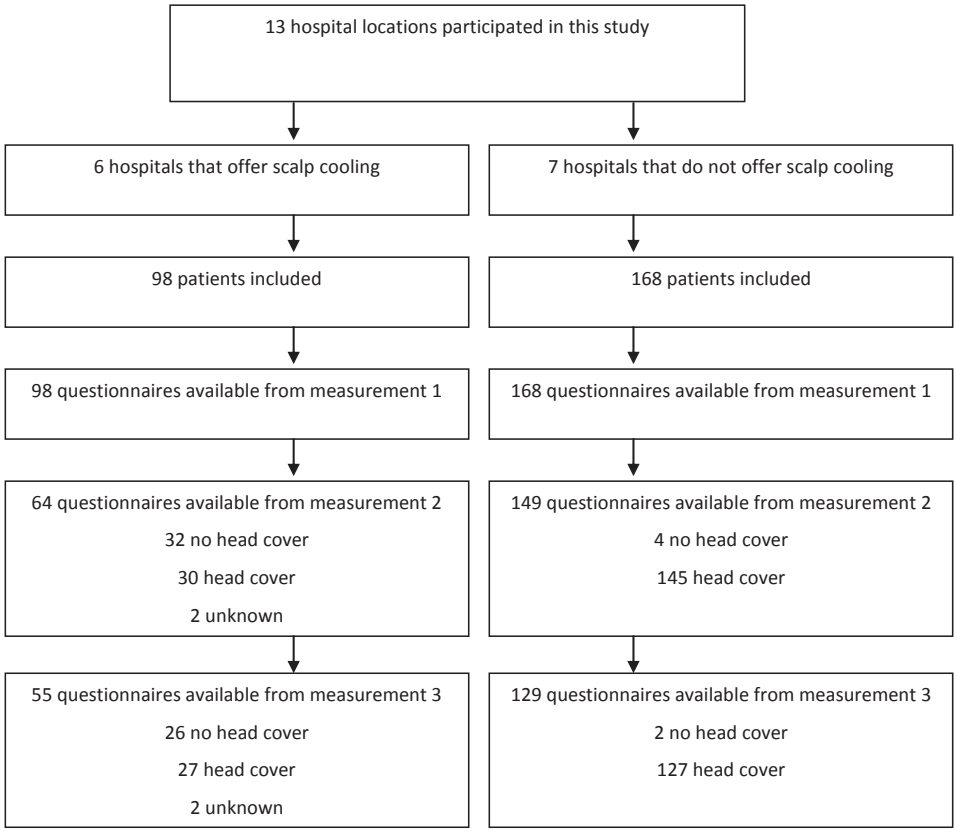


**Figure 1.** Flow-chart of the data collection process.

(range 30 to 100). Patients who did not receive scalp cooling obtained the highest rating, namely a mean of 85 (range 9 to 100). These differences in self-reported VAS scores were statistically significant for the successfully scalp-cooled group versus both other groups of patients (p<0.0001).

Extent of alopecia was also indicated by patients on the WHO scale. The mean WHO score among successfully scalp-cooled patients three weeks after chemotherapy was 1.4 (range 0 to 3) while not successfully scalp-cooled patients had a mean rating of 2.6 (range 2 to 3) and patients who had not received scalp cooling scored a mean of 2.9 (range 2 to 3). These three means differed significantly (p<0.001).

## Impact of side effects of chemotherapy and consequences of cancer

Before the onset of chemotherapy, patients expected that fear of metastases would have the highest impact on their lives, followed by alopecia and total mastectomy (Table 2). The only significant difference between the scalp-cooled and non scalp-cooled patients was seen for changes in relationship with children (42 vs. 24; p=0.003).
Three weeks and six months after the last chemotherapy, the actually experienced impact rankings were again highest for fear of metastases, alopecia and total mastectomy, although the order slightly changed compared to before chemotherapy (Table 3). Six months after completing chemotherapy a new prominent item (rank 2) was early hot flashes in the scalp-cooled group who needed head covering. The only significant group difference was found

**Table 1.** Socio-demographic and clinical characteristics of breast cancer patients treated with or without scalp cooling before the start of chemotherapy.

| | **n** (%) | | |
|---|---|---|---|
| | **Scalp cooling** (n=98) | **No scalp cooling** (n=168) | **p-value** |
| **Mean age at time of survey** | 49.8 | 49.7 | 0.68 |
| **Surgery** | | | |
| Mastectomy | 43 (44) | 94 (56) | 0.16 |
| Partial mastectomy | 50 (51) | 68 (40) | |
| **Lymph node dissection**[a] | | | |
| Yes | 79 (81) | 129 (77) | 0.42 |
| No | 15 (15) | 35 (21) | |
| **Marital status** | | | |
| Married | 76 (78) | 124 (74) | 0.31 |
| Not married/divorced | 11 (11) | 29 (17) | |
| Living together | 11 (11) | 13 (8) | |
| **Education level**[b] | | | |
| Low | 42 (43) | 91 (55) | 0.16 |
| Medium | 31 (32) | 42 (26) | |
| High | 24 (25) | 31 (19) | |
| Missing | 1 (1) | 4 (2) | |

[a] including sentinel node dissection
[b] education: low=up to the end of high school, high=bachelor and master degree

for fatigue between the scalp-cooled patients in whom hair was preserved and the non scalp-cooled patients at three weeks following the last chemotherapy (37 vs. 59; p=0.01).

## Health related quality of life

Before chemotherapy no statistical significant differences were found in HRQOL between patients with and without scalp cooling, except for cognitive functioning on the EORTC-QLQ-C30 (mean 85.9 vs. 80.7; p=0.05).

Three weeks after the last chemotherapy successfully scalp-cooled patients reported statistically significant more appetite in comparison with scalp-cooled patients who needed head covering (mean 16.7 vs. 39.1; p=0.008) (Table 4). In addition, a statistically significant

**Table 2.** Expected impact and ranking of side effects of chemotherapy and consequences of cancer one week prior to chemotherapy in patients treated with or without scalp cooling.

| | **Scalp cooling** (n=98) | | **No scalp cooling** (n=168) | |
|---|---|---|---|---|
| | **Impact**[a] | **Rank** | **Impact**[a] | **Rank** |
| Fear of metastases | 73 | 1 | 70 | 1 |
| Alopecia | 70 | 2 | 65 | 2 |
| Total mastectomy | 58 | 3 | 56 | 3 |
| Fatigue | 46 | 4 | 49 | 4 |
| Consciousness of one's vulnerability | 45 | 5 | 45 | 6 |
| Nausea | 42 | 6 | 43 | 7 |
| Arm problems | 42 | 7 | 48 | 5 |
| Changes in relationship with children | 42* | 8 | 24* | 23 |
| Vomiting | 40 | 9 | 41 | 8 |
| Breast changes through mastectomy | 35 | 10 | 37 | 9 |
| Changes in relationship with partner | 35 | 11 | 31 | 13 |
| Concentration problems | 33 | 12 | 30 | 14 |
| Mouth problems | 32 | 13 | 33 | 10 |
| Sleeping difficulties | 32 | 14 | 30 | 15 |
| Early hot flashes | 32 | 15 | 31 | 11 |
| Scalp cooling | 31 | 16 | - | - |
| Loss of appetite | 30 | 17 | 27 | 17 |
| Mood changes | 30 | 18 | 31 | 12 |
| Constipation | 29 | 19 | 26 | 19 |
| Changes in relationship with friends | 27 | 20 | 24 | 20 |
| Burning eyes | 27 | 21 | 24 | 21 |
| Skin problems | 27 | 22 | 26 | 18 |
| Change in taste | 27 | 23 | 29 | 16 |
| Difficulties taking care of oneself | 26 | 24 | 23 | 24 |
| Diarrhea | 25 | 25 | 24 | 22 |
| Nail problems | 14 | 26 | 14 | 25 |

* significant difference at <0.05

[a] impact= the mean score people gave to a item (range 0-100)

difference was found for complaints about alopecia between scalp-cooled patients who required a head cover and the non scalp-cooled group (mean 43.7 vs. 25.2; p=0.02). Overall, a trend was observed for better HRQOL in successfully scalp-cooled patients, whereas the unsuccessfully scalp-cooled group tended to have the worst HRQOL.

## Body image

Before chemotherapy, patients who were about to have scalp cooling reported more concern about body appearance (mean 3.27 vs. 3.02; p=0.03) and a somewhat higher importance for hair (mean 4.43 vs. 4.25; p=0.06) compared to patients who were not treated with scalp cooling (Table 5). Three weeks after completing chemotherapy, successfully scalp-cooled

**Table 4.** QLQ-C30 and QLQ-BR23 three weeks after completing chemotherapy in patients treated with and without scalp cooling.

| | **Scalp-cooled, no head cover** (n=32) | | **Scalp-cooled, head cover** (n=30) | | **No scalp cooling** (n=145) | |
|---|---|---|---|---|---|---|
| | **Mean** (sd) | | **Mean** (sd) | | **Mean** (sd) | |
| **EORTC-QLQ-C30** | | | | | | |
| Global health status/QOL | 68.5 | (21.7) | 60.3 | (22.2) | 63.9 | (21.8) |
| Physical function | 77.9 | (19.4) | 70.7 | (16.3) | 74.4 | (19.2) |
| Role function | 62.0 | (31.5) | 52.2 | (24.3) | 56.3 | (29.0) |
| Emotional function | 72.1 | (23.1) | 67.8 | (22.8) | 70.2 | (23.2) |
| Cognitive function | 72.4 | (26.6) | 65.0 | (28.8) | 69.6 | (25.6) |
| Social function | 79.7 | (24.6) | 71.7 | (24.0) | 72.1 | (26.2) |
| Fatigue | 42.7 | (28.4) | 54.4 | (25.3) | 51.8 | (26.1) |
| Nausea and vomiting | 17.2 | (18.7) | 27.0 | (30.3) | 24.7 | (29.0) |
| Pain | 13.5 | (18.7) | 17.8 | (25.5) | 20.3 | (24.1) |
| Dyspnea | 20.8 | (23.6) | 27.8 | (27.8) | 26.6 | (30.2) |
| Sleep disturbance | 33.3 | (29.3) | 37.8 | (28.7) | 34.5 | (33.1) |
| Appetite | 16.7 | (26.8)* | 39.1 | (36.8)* | 27.1 | (29.2) |
| Constipation | 17.7 | (25.4) | 24.1 | (23.4) | 23.2 | (29.4) |
| Diarrhea | 9.4 | (19.4) | 8.0 | (17.0) | 7.5 | (17.9) |
| Financial impact | 13.5 | (26.6) | 18.9 | (28.6) | 12.9 | (24.4) |
| **EORTC-QLQ-BR23** | | | | | | |
| Body image | 74.2 | (27.9) | 65.3 | (23.4) | 71.4 | (26.8) |
| Sexual function | 28.0 | (26.0) | 23.6 | (20.2) | 21.8 | (19.7) |
| Sexual enjoyment[a] | 54.2 | (26.9) | 48.1 | (17.0) | 54.5 | (26.4) |
| Future perspective | 53.8 | (30.6) | 52.2 | (25.8) | 51.0 | (30.1) |
| Breast symptoms | 31.0 | (19.2) | 41.0 | (18.1) | 39.2 | (18.2) |
| Arm symptoms | 19.0 | (18.7) | 21.9 | (23.7) | 18.0 | (19.2) |
| Systemic therapy side effects | 20.8 | (22.5) | 18.1 | (20.1) | 20.6 | (18.9) |
| Alopecia | 21.8 | (31.2) | 43.7 | (40.0)* | 25.2 | (37.5)* |

*significant difference at <0.05

[a] compliance with item sexual enjoyment is only 50%

**Table 3.** Experienced impact and ranking (rank 1 to 5) of side effects of chemotherapy and consequences of cancer three weeks and six months after completing chemotherapy in patients treated with or without scalp cooling.

| | 3 weeks after completing chemotherapy | | | | | | 6 months after completing chemotherapy | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Scalp-cooled, no head cover (n=32) | | Scalp-cooled, head cover (n=30) | | No scalp cooling (n=145) | | Scalp-cooled, no head cover (n=26) | | Scal- cooled, head cover (n=27) | | No scalp cooling (n=127) | |
| | Impact[a] | Rank | Impact | Rank | Impact | Rank | Impact | Rank | Impact | Rank | Impact | Rank |
| Alopecia | 68 | **1** | 63 | **1** | 67 | **1** | 62 | **1** | 57 | **1** | 58 | **2** |
| Fear of metastases | 66 | **2** | 57 | **2** | 60 | **3** | 50 | 4 | 51 | 6 | 64 | **1** |
| Arm problems | 65 | **3** | 32 | 15 | 47 | 7 | 49 | 7 | 42 | 10 | 51 | 6 |
| Total mastectomy | 62 | 4 | 50 | 4 | 65 | 2 | 54 | **3** | 53 | **3** | 56 | **3** |
| Consciousness of one's vulnerability | 48 | 5 | 48 | 5 | 47 | 6 | 55 | **2** | 37 | 12 | 49 | 7 |
| Fatigue | 37* | 7 | 56 | **3** | 59* | **4** | 45 | 8 | 53 | 5 | 52 | 5 |
| Nausea | 33 | 9 | 47 | 6 | 51 | 5 | 37 | 13 | 53 | 4 | 43 | 9 |
| Trouble sleeping | 21 | 13 | 26 | 18 | 41 | 11 | 50 | 5 | 46 | 8 | 40 | 11 |
| Early hot flashes | 12 | 19 | 36 | 12 | 42 | 10 | 50 | 6 | 54 | **2** | 55 | 4 |

*significant difference at <0.05

[a] impact= the mean score people gave to a item (range 0-100)

**Table 5.** Body image one week prior to chemotherapy and three weeks after chemotherapy among patients treated with and without scalp cooling.

| | Before chemotherapy | | | 3 weeks after completing chemotherapy | | | |
|---|---|---|---|---|---|---|---|
| | Scalp cooling | No scalp cooling | | Scalp-cooled, no head cover | Scalp-cooled, head cover | No cooling, head cover | |
| | Mean (sd) | Mean (sd) | p-value | Mean (sd) | Mean (sd) | Mean (sd) | p-value |
| **Body image (BIS)** (range 0-30) | | | | | | | |
| Total score | 7.71 (4.97) | 7.24 (5.76) | 0.51 | 9.13 (6.00) | 12.18 (5.94) | 9.74 (5.93) | 0.10 |
| **Concern about body image (MBA)** (range 1-5) | | | | | | | |
| Concern about appearance | 3.27 (0.76) | 3.02 (0.89) | **0.03** | 2.97 (0.88) | 3.23 (0.91) | 3.08 (0.87) | 0.20 |
| Concern about body integrity | 2.59 (0.89) | 2.49 (1.02) | 0.44 | 2.59 (1.00) | 3.02 (0.99) | 2.66 (0.96) | 0.91 |
| **Importance of hair for body image** (range 1-5) | | | | | | | |
| My hair is important to me | 4.43 (0.83) | 4.25 (0.83) | 0.06 | 4.09 (0.86) | 4.50 (0.63) | 4.27 (0.81) | **0.01** |
| My hair is important for my appearance | 4.25 (0.68) | 4.09 (0.93) | 0.15 | 3.94 (0.84) | 4.40 (0.62) | 4.14 (0.86) | 0.07 |

patients reported that their hair had a significant lower importance for their body image (mean 4.09; sd 0.86) compared to scalp-cooled patients who needed head covering (mean 4.50; sd 0.63) and patients not treated with scalp cooling (mean 4.27; sd 0.81) (p=0.01).

### Depression and anxiety

Before chemotherapy, no statistically significant differences were found in anxiety and depression between patients who were about to have scalp cooling and those who were not (depression 3.67 vs. 4.11; p=0.19 and anxiety 5.69 vs. 5.22; p=0.83). In addition, no statistically significant differences were found three weeks after the last chemotherapy between successfully and unsuccessfully scalp-cooled patients and the non scalp-cooled group (depression 3.23 vs. 4.29 vs. 4.10; p=0.40 and anxiety 5.32 vs. 5.89 vs. 5.22; p=0.73).

## Discussion

This is the first study designed to assess the effect of scalp cooling on well-being. A trend to better well-being was found in successfully scalp-cooled patients, as evidenced by a general better HRQOL and a better body image. On the other hand, unsuccessfully scalp-cooled patients reported significantly more complaints about alopecia and a tendency to less well-being compared to non scalp-cooled patients. However this was not reflected in higher anxiety or depression scores. Furthermore, this study revealed that the large majority of patients expected alopecia to be among the most distressing problems of chemotherapy and this side effect remained one of the most distressing problems three weeks as well as six months after completing chemotherapy.

It is tempting to speculate about explanations for the observed group differences in alopecia and well-being. From a psychological point of view, the uncertainty regarding hair preservation in scalp-cooled patients may cause additional distress (E. Boot, unpublished observations) and severe alopecia despite scalp cooling may lead to extra disappointment. However, an alternative or concomitant explanation for the differences in well-being is physiological in nature; maybe unsuccessfully scalp-cooled patients have a greater biological availability of cytostatics. This hypothesis is supported by the additional report of more hot flashes, more fatigue, more nausea and less appetite in unsuccessfully scalp-cooled patients in comparison with successfully and non scalp-cooled patients. Moreover, it could explain their alopecia despite scalp cooling.



The present study revealed only a trend towards somewhat better HRQOL and body image in the successfully scalp-cooled patients in comparison with unsuccessfully and non cooled patients. The lack of significance may be caused by insensitivity of the measurement instruments, as the applied questionnaires were not developed to measure differences in HRQOL and body image with respect to alopecia. On the other hand, the finding of significance may be caused by chance in multiple testing. In addition, it is not clear to what extent wearing wigs and head covering reduces distress. In a few previous studies HRQOL and body image have been negatively associated with alopecia, as has been shown in a recent review.[29]

Although patients who had chosen for scalp cooling reported more concern about their appearance before chemotherapy than non scalp-cooled patients, they did not correctly

predict the importance of hair for body image. The importance became particular evident after having completed chemotherapy, especially in patients who ultimately had experienced alopecia despite scalp cooling. Before starting chemotherapy, the non scalp-cooled patients maybe had hope [30-32] but hardly expectations on preservation of their hair, because the chemotherapy schedules administered in this study nearly always cause severe alopecia. Since these patients anticipated alopecia, they might have been more prepared for this side effect and its impact on their appearance. Even though, also in the literature describing non scalp-cooled patients, it is has been repeatedly reported that the experience of alopecia is very upsetting.[3,32-34] This stresses the need of extra support for patients experiencing alopecia[30], especially since physicians and nurses tend to underestimate its impact.[4,5]

Before chemotherapy, a significant difference was found for the impact of chemotherapy and cancer on the relationship with children, between patients who were or were not about to have scalp cooling. Maybe particularly women with children choose scalp cooling when it is offered to them, in order to prevent their children from being confronted with their baldness. However, after chemotherapy no significant differences were observed in relationships with children between patients with or without alopecia, so probably patients' anticipated concerns about the relationship with their children were overrated. Moreover, patients reported that their young children adapted quickly to their changed appearance. As far as known, the impact of alopecia on relatives has not been studied until now.

Alopecia prevention was defined on the basis of the patient's opinion that their hair was preserved to such an extent that no wig or head covering was needed. This is justified by the fact that WHO and VAS scores, both pretending to represent the actual loss of hair, were associated insufficiently with each other and with the use of head covering and therefore appear to be less appropriate. However, it is known that the patient's decision to wear a wig or head cover will not always be directly related to the severity of alopecia; some patients with minimal alopecia nevertheless experience it as a severe burden and choose to wear a head cover, and the opposite is also true. A simple objective quantification of alopecia in order to evaluate the effectiveness of various methods of scalp cooling would be most helpful. In future studies, perhaps Cohen's trichometer might be suitable.[35] But, ultimately, it should be the patients' appraisal of the result of scalp cooling that must be perceived as most important.

This study has some limitations. Firstly, patient selection might have occurred, which might have biased the results on well-being, particularly in hospitals practising scalp cooling. It is not known what percentage of patients was eligible, had been offered scalp cooling and subsequently had chosen for scalp cooling. Patient characteristics in scalp-cooled and non scalp-cooled patients did not differ, however the response rate was lower in scalp-cooled patients. In addition, although the TAC regimen is tougher than AC, FEC and FAC, is not expected that the applied chemotherapy regimens will have caused differences in outcome between the subgroups of patients, because TAC was hardly administered (<5%) to breast cancer patients in the scalp cooling hospitals in 2005 and 2006. Only minimal bias may have occurred by assigning patients who stopped scalp cooling as a result of intolerance to the subgroup of unsuccessful scalp-cooled patients, because in literature this number is hardly

more than 10%.[20] Finally, because the non scalp-cooled group may also contain patients who would have chosen scalp cooling if it was offered in their hospital, the differences before chemotherapy might be underestimated, in particular for body image. Secondly, a limitation of the present study is the relatively large number of drop outs, which are mainly due to administrative issues. In future studies, more attention should be given to data collection in the hospitals.

Over the past decades, the impact of chemotherapy-induced side effects has changed considerably[6], mainly due to changes in treatment, including symptom management. For example, medication against nausea and vomiting has improved, therefore these side effects became less important in comparison to other side effects that can not be minimised or prevented. With respect to alopecia, the quality of wigs has improved, the possibilities for head covering are meanwhile extensive and patients are nowadays regularly advised about managing alopecia before starting chemotherapy. Nevertheless, it remains an important issue for patients, which deserves attention for research.[29,31,32] In the prevention of alopecia, the unanswered question remains whether or not the possible positive effects for successfully scalp-cooled patients outweighs the possible negative effects when scalp cooling is unsuccessful. The answer will be mainly determined by the effectiveness of scalp cooling in a particular chemotherapy regimen. Therefore, efforts have to be undertaken to further improve the results of scalp cooling and it should not be offered to patients when the chance of hair preservation is minimal. The effectiveness of scalp cooling can only be determined when results are systematically registered, which is nowadays, as far as we know, only applied on a large scale in the Netherlands.

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