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BRIEF REPORT

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# PULSED ELECTROSTATIC FIELDS (ETG) TO REDUCE HAIR LOSS IN WOMEN UNDERGOING CHEMOTHERAPY FOR BREAST CARCINOMA: A PILOT STUDY

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## SUMMARY

**Aims:** To determine whether specific pulsed electrostatic fields, or electrotrichogenesis (ETG), could potentially prevent or reduce hair loss in patients undergoing adjuvant cyclophosphamide, methotrexate and 5-fluorouracil (CMF) chemotherapy for breast cancer.

**Methods:** Thirteen women were followed during their adjuvant ETG and chemotherapy treatment to determine the efficacy of ETG. All patients were treated for 12 min, twice weekly with a pulsed electrostatic field. Quantitative hair loss was measured by photographic assessment, and manual hair count. Quality of life assessment was conducted at the end of the study.

**Results:** Twelve out of 13 participants had good hair retention throughout the chemotherapy period and afterwards. There were no reported side effects attributable to ETG.

**Conclusions:** This study shows encouraging results in an area where no other appropriate treatment is available. Reducing alopecia, secondary to chemotherapy has the potential to increase CMF treatment compliance, enhance patient self-esteem, and improve overall quality of life during this stressful period. Copyright © 2002 John Wiley & Sons, Ltd.

## INTRODUCTION

Cyclophosphamide, methotrexate and 5-fluorouracil (CMF) chemotherapy for breast cancer is one of the regimes used in New Zealand, and this combination, particularly cyclophosphamide and 5-fluorouracil, are responsible for hair loss in 56–90% of patients undergoing therapy (Fisher *et al.*, 1990, Sitzia and Huggins 1998, Pronzato *et al.*, 1987). In one study (Sitzia and Huggins 1998), patients had a mean severity of 50% hair loss. Hair loss during treatment can result in significant psychological trauma.

Breast cancer diagnosis and subsequent therapy may elicit responses such as depression, anxiety, hostility, decreased self-esteem, hopelessness, denial and loss of control (Rabinowitz and Adler, 1998). Some women perceive hair loss as worse than losing a breast to surgery because it is such a visible loss. Studies report that for 46% of women undergoing chemotherapy, alopecia was the most traumatic side effect of chemotherapy, and 73% of these women never regained their self confidence even after the regrowth of hair (Munstedt *et al.*, 1997; Weiss and Wejss 1997).

Current treatment options are limited. Cold caps are no longer considered appropriate therapy, because many oncologists believe they may provide a sanctuary for malignant cells (Witman *et al.*, 1981). Wigs may be expensive or unsatisfactory for other reasons. Minoxidil does not prevent hair

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loss, although it does shorten the period of baldness following chemotherapy (Duvic *et al.*, 1996). Clearly, a better approach would be welcome.

The therapeutic benefits of various electromagnetic fields have recently been well documented. Pulsed electromagnetic fields (PEMF) are employed as adjunctive therapy for a variety of musculoskeletal injuries (Pilla, 1993). Perhaps the most widely known PEMF application is in current orthopaedic clinical practice for the treatment of delayed and non-union fractures. The pulsed electrostatic signal employed in this study, Electrotrichogenesis (ETG) is similar to that employed by other PEMF devices, except it is applied via metal plates placed at a fixed distance in air from the scalp. In a controlled clinical trial to examine safety and efficacy of ETG in men with androgenetic alopecia, Maddin *et al.* (1990, 1992) demonstrated a positive biologic effect on hair regrowth.

The ETG modality is quite distinctly different from other electrotherapeutic modalities, and no direct confirmation of ETG 'mechanism' at the cellular level is presently available. Though ETG design parameters have been judiciously selected, direct clinical evidence for optimization of these parameters is not yet available due to the very large scale of clinical effort which such multi-parameter optimization would require.

The current pilot study explored the use of this therapeutic modality in women undergoing adjuvant CMF chemotherapy for the treatment of breast cancer to determine whether ETG could prevent or reduce hair loss.

## METHODS

The study group was open to women aged 19–65 years with a clinical diagnosis of breast cancer and who were awaiting CMF chemotherapy, but otherwise in good health. All patients were investigated at a specialist breast centre in Auckland, New Zealand. The treatment protocol had ethical review and approval. All subjects gave informed consent.

Subjects ( $n=14$ ) were screened by a physician investigator (TM) and trained on a hair collection technique defined by the Ethics Committee using a standard hairbrush. Following shampooing, on the day of their ETG treatment, each subject

brushed from the front crown to the nape of the neck using five strokes. Nursing staff then removed all hairs from the brush and deposited them in labelled receptacles. An independent registered nurse then qualified and recorded weekly hair counts for each patient. All subjects used their personal hair care routines between ETG treatments.

At each visit, subjects were provided with a clean brush, gave self-reports of any symptoms, complaints and concomitant medications, and had five photographs (top, left, right, front, and back of head views) taken.

The ETG electric field comprises brief pulses of duration on a millisecond time scale, repeated several times per second. The ETG electrode array has been designed to provide an appropriate geometric distribution of electric field at the scalp surface, while minimizing the field exposure inferior to the scalp, as well as below the cranial hair area. The pulsed ETG signal is applied via insulated copper (metal) plates placed at a fixed distance in the air from the scalp using a hood to position the head relative to the electrodes. No active element is, thus, in contact with the scalp. The subject sits under the hood for a 12-min treatment session, during which no physical sensation is experienced.

The chemotherapy protocol was the standard CMF protocol comprising six consecutive 4-week cycles. Some minimal departures from this are unavoidable due to intercurrent illness of some subjects. Each cycle consisted of Cyclophosphamide 150 mg taken orally day 1 through 14; Methotrexate 50–75 mg and 5FU 900–1100 mg given intravenously on days 1 and 8; no chemotherapy on days 15–28. Cyclophosphamide, taken orally, has been associated with greater prevalence of hair loss (Fisher *et al.*, 1990). Completion of the protocol occurred in 100%.

The ETG protocol comprised 12-min ETG treatment administered twice weekly for 6 weeks, two days apart starting 2 weeks prior to chemotherapy. Then followed by treatments once per week for 12 weeks, twice weekly for 2 more weeks, and finally, once per week for 6 weeks after completion of chemotherapy. All but one subject complied with the RTG treatment schedule, and that subject was deleted from the analysis due to travel outside the country.

Efficacy assessments included photographs, quantitative assessment of hair loss; and subject, investigator and nurse's global assessments of hair

loss. The global assessments used a four-point scale: slight increase, same amount of hair, slight decrease, total hair loss. They were done every six weeks and compared to baseline.

## RESULTS

Of the fourteen women enrolled, the mean age was 43 (25–59). In addition to chemotherapy, all had undergone previous surgery and some had undergone chest and axillary radiotherapy. Thirteen subjects were evaluated. One withdrew due to non-compliance.

Quantitative assessments were performed each week by counting of the number of hairs collected in each brush. The hair collection method used in this study produced an average of nine hairs in the brush at the first hair count. During chemotherapy treatment nine of 13 subjects had low numbers (<40) of hairs in the brush. The remaining four subjects had higher numbers (>80) of hairs in the brush during chemotherapy. Hair counts for all subjects returned to the pre-chemotherapy rate at the end of the treatment period.

The global assessments made by the subject, nurse, and a physician investigator (the assessors) were conducted independently, but all were in agreement in terms of their observations (Table 1). At the study endpoint, for 5/13 subjects, the assessors reported a slight decrease in the amount of hair when compared to baseline. For 7/13 subjects, assessors reported the same amount of hair as before treatment, and for 1/13 subjects a slight increase in the amount of hair compared to baseline.

Photographic assessments were done by a physician investigator. When compared to baseline, the end point photographs showed the same

Table 1. A four point scale was used to determine assessment of hair loss. All assessors were in agreement when comparing endpoint results to baseline

Global assessment 4-Point Scale	Physician investigator	Nurse	Subject
Slight increase	1	1	1
Same amount	7	7	7
Slight decrease	5	5	5
Total hair loss	0	0	0

Table 2. An 11 point Likert-type scale, ranging from –5 (extremely ineffective) to 5 (extremely effective) with 0 indicating no change, was used to measure efficacy and quality of life for all the subjects

Scale	Efficacy	Quality of life
5	17%	25%
4	50%	58%
3	25%	17%
2	8%	0
1	0	0
0	0	0
–1	0	0
–2	0	0
–3	0	0
–4	0	0
–5	0	0

amount of hair for 8/13 subjects, while 4/13 showed an increase of hair. The 13th subject showed some decrease in the amount of hair.

The subjects participated in a quality of life assessment. They were asked to provide their opinion of the efficacy of ETG and assess their quality of life and sense of well-being during the trial. Twelve of the 13 subjects participated. An 11 point Likert-type scale, which ranged from –5 (extremely ineffective) to 5 (extremely effective) with 0 indicating no change, was used. Results of these two assessments indicated all subjects responding felt that a mean value of 4 accurately described both ETG efficacy and quality of life suggesting ETG treatments had a positive impact on quality of life (Table 2).

There were no reported side effects attributable to ETG treatment.

## DISCUSSION

Alopecia, secondary to chemotherapy, is a major cause of negative changes to self-concept and body image (Weiss and Weiss, 1997; Baxley *et al.*, 1984). For some women hair loss is perceived as being worse than losing a breast it is such a visible loss. Studies reported that for 46% of women alopecia was the most traumatic side effect of chemotherapy and 73% of these women never regained their self-confidence even after the regrowth of hair (Pickard-Holley, 1995). Apart from feelings of insecurity, the loss of identity can generate a sense of hopelessness and can result in a loss of the

effectiveness of medical treatment (Munstedt *et al.*, 1997; Pickard-Holley, 1995; Baxley *et al.*, 1984).

A diagnosis of breast cancer and its ensuing treatment have become the focus of increasing attention in recent years. Depression, anxiety, hostility decreased self-esteem, hopelessness, denial, loss of personal control have all been identified as common responses to breast cancer (Rabinowitz *et al.*, 1998).

To date, there has been no satisfactory solution to the problem. At a time when women must cope with many other overwhelmingly negative factors associated with the diagnosis and treatment of breast cancer, anticipated hair loss is a genuine fear (Baxley *et al.*, 1984; Lindley *et al.*, 1999), only partially ameliorated by the use of a wig.

Overall, the several independent measures employed in this pilot study showed 12 of 13 subjects (92%) treated with conventional CMF chemotherapy and ETG experienced negligible alopecia throughout the course of treatment and afterwards. There was no evidence of delayed alopecia. This is substantially different from the 50% hair loss reported for approximately 50% of patients undergoing conventional CMF chemotherapy, and from the 15% who experienced complete hair loss (Fischer *et al.*, 1990).

Although the sample size in this pilot study is small, 13 subjects, a modal calculation performed for statistical power using SigmaStat 2.0 (SPSS, Inc.) suggests the mean loss in ETG treated patients is statistically significantly different from that normally reported during CMF therapy using either a standard *t*-test or ANOVA. To illustrate, the mean hair loss for a group of patients undergoing standard CMF therapy was assumed to be  $50 \pm 20\%$ , (Fisher *et al.*, 1990). The mean hair loss for the 13 subjects treated with ETG can be conservatively taken as  $15 \pm 6\%$ , as determined from all three measured employed to assess hair loss in this study and assuming the same high standard deviation ( $\pm 0.4$ ). The difference in the means for the two groups is then  $35 \pm 14\%$  (to a first approximation). The sample size required for the difference in mean hair loss to be significant to  $P < 0.05$  (for power = 1) is 12 (12), and, for power = 0.8 (limit of confidence), seven (7). Both sample numbers are less than the total of 13 subjects in this study. This is not unexpected given that hair loss was observed to be negligible ( $< 15\%$ ) in 12 of 13 subjects (92%), with one subject experiencing approximately 50% hair loss.

ETG efficacy in reducing hair loss caused by other chemotherapy regimes is unknown. However, these results are of sufficient interest to suggest that a randomized, controlled trial be developed for CMF and that the study population might be expanded to include other chemotherapy regimes that commonly produce alopecia.

The fact that the ETG treatment was painless, convenient and simple to use was a positive aspect for the subjects. Choosing to participate in this study allowed them to maintain some control over their lives at a time when they felt control was being taken away. As a result, they reported feeling more confident about having to undergo chemotherapy, provided the ETG treatment accompanied it.

The mechanism of action for ETG on hair biology is not yet clarified. There have been many studies of various electromagnetic signals that show effects at the cellular level (Bersani, 1999). Of particular relevance are those related to direct EMF effects on  $\text{Ca}^{2+}$  binding at regulatory molecules (Pilla *et al.*, 1999).

## CONCLUSIONS

CMF chemotherapy patients undergoing concurrent ETG treatment appear to have good hair retention compared to historical data. ETG may provide a significant solution for CMF chemotherapy induced hair loss.

The complex emotional, psychological and social factors that affect the response women have to the diagnosis and treatment for breast cancer is an important component of designing and delivering services to them. In this context, this study addresses one of the side effects women fear most. The women taking part in this study, like others with breast cancer, view chemotherapy induced alopecia as undesirable and negatively impacting on their self-image.

Based upon this pilot study, randomized, double-blinded control studies should be developed to fully validate the ETG technique in preventing hair loss secondary to chemotherapy.

## ACKNOWLEDGEMENTS

The authors appreciate the assistance of Arthur Pilla, Ph.D., Mount Sinai School of Medicine, New York and

of Douglas Beder, Ph.D., Vancouver, British Columbia who provided expertise and advice with bioelectromagnetics. Special thanks are extended to the nurses, Jo-Ann Blomfield, R. Comp. N, B.H.Sc., and Ruth Hunt, R.N., Cert, P.N. This study was supported, in part, by a grant from Current Technology Corporation, Vancouver, Canada.

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