Reducing chemotherapy-induced hair loss with cold caps

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Chemotherapy Induced Hair Loss

• Temporary hair loss is one of the most distressing and traumatic side effects of chemotherapy

• Women with chemotherapy induced alopecia report:
  – lower self-esteem
  – poorer body image
  – lower quality of life

• Hair loss impacts patients’ decision to accept or decline chemotherapy
  – As many as 8% may decline chemotherapy due to risk of alopecia

Munstedt K et al. Support Care Cancer, 1997; McGarvey EL et al. Clinical Prac, 2001
Strategies Employed to Reduce or Prevent Hair Loss

- **Scalp tourniquet** (Pesce A et al NEJM 1978)

- **Topical minoxidil** (Duvic M et al J Am Acad Derm 1996)

- **Scalp cooling**
  
<table>
<thead>
<tr>
<th>Tourniquets (bands)</th>
<th>Ice Caps (crushed ice)</th>
<th>SCSII system</th>
<th>DigniCap</th>
</tr>
</thead>
<tbody>
<tr>
<td>60s</td>
<td>70s</td>
<td>80s</td>
<td>90s</td>
</tr>
<tr>
<td>Penguin</td>
<td>Elasto-Gel</td>
<td>Paxman coolers</td>
<td>2000 onwards</td>
</tr>
</tbody>
</table>
Rationale for Scalp Cooling

• Vasoconstriction\(^1\)
  – Reduces the blood flow to hair follicles during peak plasma concentrations of chemotherapy
  – Reduces cellular uptake of chemotherapy

• Reduced biochemical activity\(^2\)
  – Makes hair follicles less susceptible to damage from chemotherapeutic agents

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2. Lundgren-Eriksson et al, Eur J Cancer 1999
Scalp Cooling

• Scalp cooling
  – Widely used internationally
  – Recent increase in prospective trials
  – Most potentially effective method to prevent hair loss

• Caveats:
  – Past studies were generally small and poorly designed
  – Considerable variation in success rates reported
  – Variables include
    • Cooling time
    • Type, duration, and dose intensity of chemotherapy
    • Temperature and temperature maintenance
Penguin Cold Cap

- Patented, insulated cap
- Fits all sizes of heads
- Manufactured with gel designed to remain soft and pliable in extremely cold temperatures
- Fitted in place with six velcro straps
Cold Cap Specifications

• Made from white medical grade hypo-allergenic polyurethane
• Filled with a special patented formula crylon gel with an insulated blue nylon cover
• All materials used in the manufacturing of the caps are approved by the FDA in the USA (but the cap is not FDA approved)
Penguin Cold Cap

• The cap is non toxic, hypoallergenic and can be disinfected
• It is soft and pliable, even in extremely cold temperatures.
• Weight: 1.5kg / 3 lbs
Cooling the Cap

• To achieve maximum success, the Penguin Cold Caps must be cooled in a freezer or on dry ice to the correct temperature before use.

• Caps must be stored in the freezer for 24 hrs before their use depending on the cooling capacity of the freezer:
  – Freezer must be able to cool to -35°C.
Practical Use of the Penguin Cold Cap

• The cap is placed on the head before the start of chemotherapy to allow the scalp to cool

• Caps are changed on a regular basis
  – The first two Cold Caps are worn for 20 minutes each
  – All subsequent Cold Caps are worn for 30 minutes
  – Patients continue to change the Cold Caps for 2-3 hours after the completion of chemotherapy infusion

• The number of Cold Cap’s required is dependent on:
  – Hair thickness
  – Duration of chemotherapy administration
  – Guidance is given as to the number of caps required based on the patient
DigniCap

- System consists of a tight-fitting silicon cooling cap with circulating coolant and temperature sensors connected to the cooling and control unit.

- Liquid coolant circulates through tunnels in the inner cap.

- An outer neoprene insulating cap is used for insulation and securing fit of inner cap.
Paxman Cooling System

• Unit
  – Refrigeration unit weighing 30kg

• Caps
  – Color coded, lightweight silicone caps with insulating neoprene cap
  – Provided in a range of sizes to suit varying individual patient heads
Scalp Cooling Procedure

- **Fitting of the cap:**
  - **PRECOOLING TIME:** 20-30 min

- **Scalp cooling:**
  - **INFUSION TIME:** x min

- **Post cooling time:**
  - **POST COOLING TIME:** 30 - 120 min*

**Premedication**
- Drug infusion start
- Drug infusion end
Scalp Cooling Review – Era 2005

- 53 publications and three personal communications between 1973-2003

- In 6 of 7 randomized studies, a significant improvement in hair preservation was seen with scalp cooling
  - One randomized study after 1995 showed (marginal) positive results with epirubicin and docetaxel

- Positive results reported in 13 out of 14 non-randomized studies with historical controls

- In 35 studies without historic controls, 31 showed positive results

## Review of Randomized Trials

<table>
<thead>
<tr>
<th>No. of cooled patients</th>
<th>No. of controls</th>
<th>Chemotherapy agents and doses (mg/m²)</th>
<th>% patients with good(^a) hair preservation (controls)</th>
<th>(P) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>40</td>
<td>37</td>
<td>D50, Vc(^b), F500, 4 × p.o.: M20 + Ch40</td>
<td>50% (19%)</td>
<td>(P &lt; 0.05)</td>
</tr>
<tr>
<td>19</td>
<td>16</td>
<td>Combinations including D30-70</td>
<td>37% (0%)</td>
<td>(P &lt; 0.025)</td>
</tr>
<tr>
<td>10</td>
<td>9</td>
<td>D31-125(^b), C300–800(^b)</td>
<td>10% (0%)</td>
<td>NS</td>
</tr>
<tr>
<td>15</td>
<td>15</td>
<td>E75, DT75</td>
<td>25% (0%)</td>
<td>(P = 0.001–0.012^c)</td>
</tr>
<tr>
<td>6</td>
<td>6</td>
<td>C600, M40, F600</td>
<td>100% (17%)</td>
<td>(P &lt; 0.01)</td>
</tr>
<tr>
<td>19</td>
<td>16</td>
<td>C600, M40, F600</td>
<td>85% (63%)</td>
<td>(P = 0.014^d)</td>
</tr>
<tr>
<td>12</td>
<td>13</td>
<td>D20-60 multiple combinations</td>
<td>75% (8%)</td>
<td>(P = 0.0009)</td>
</tr>
</tbody>
</table>

\(^a\)WHO grade 0, 1, 2 unless in the opinion of the authors the hair preservation in a part of the patients with grade 2 is not good or if the authors mention ‘good hair preservation’, or ‘no wig required’.

\(^b\)Doses not per m².

\(^c\)Depending on who rated hair loss: patients, nurses or experts.

\(^d\)\(P\) value calculated for the incidence of alopecia of any grade.

C, cyclophosphamide; Ch, chlorambucil; Cp, cisplatin; D, doxorubicin; DT, docetaxel; E, epirubicin; F, 5-fluorouracil; M, methotrexate; Vc, vincristine;
### Results Before and After 1995

<table>
<thead>
<tr>
<th>Reference</th>
<th>% patients with good hair preservationa</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean value</td>
</tr>
<tr>
<td>Studies before 1995 [3, 8–10, 12, 14, 28–46, 48–56]; 1563 cases</td>
<td>56</td>
</tr>
<tr>
<td>Studies since 1995 [1, 2, 7, 11, 13, 15–18, 20–27]; personal communication: C. Christodoulou, Athens Medical Centre, Greece; personal communication: A.D. Klaren, Albert Schweizer Hospital, Dordrecht, The Netherlands; personal communication: B. Kolen, Elisabeth Hospital, Tilburg, The Netherlands; [19]b; 1047 cases</td>
<td>73</td>
</tr>
</tbody>
</table>

- The average success rate of the studies carried out before 1995 was 56% and from 1995 onwards 73%.
- The 19 non-randomized studies carried out from 1995 onwards all showed positive results.
Penguin Cold Cap Single Institution Experience

Wills S et al, SABCS 2009
Impact of Alopecia and Scalp Cooling on the Well-Being of Breast Cancer Patients

• Prospective non-randomized multi-center study in 13 hospitals
• Breast cancer patients
  – 98 used scalp cooling with the Paxman system
  – 168 did not use scalp cooling
• Scalp cooling was effective (no need for head covering) in 52% of the cases
• Quality of life: questionnaires completed before, at 3 weeks, and 6 months after last chemotherapy
  – Trend towards greater sense of well-being in patients with ‘successful’ scalp cooling
  – Patients who lost their hair despite use of scalp cooling reported the lowest sense of well-being

## Scalp Metastases in Breast Cancer Patients in the Chemotherapy Era

<table>
<thead>
<tr>
<th>Study</th>
<th>BC patients</th>
<th>Skin Mets</th>
<th>Scalp Mets</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lookingbill, 1990</td>
<td>992</td>
<td>237 (24%)</td>
<td>NR</td>
</tr>
<tr>
<td>Lookingbill, 1993</td>
<td>707</td>
<td>212 (30%)</td>
<td>18 (2.5%)</td>
</tr>
<tr>
<td>Krathen, 2003</td>
<td>1903</td>
<td>457 (24%)</td>
<td>&lt;47 (&lt;2.5%)</td>
</tr>
<tr>
<td>Lemieux, 2009</td>
<td>87</td>
<td>NR</td>
<td>1 (1.2%)</td>
</tr>
</tbody>
</table>

# Scalp Metastases after Adjuvant Chemotherapy and Scalp Cooling

## Expert Statement on Scalp Metastases. Rugo et al, 2009

<table>
<thead>
<tr>
<th>Study</th>
<th>Breast cancer patients</th>
<th># patients w/ scalp mets with scalp cooling</th>
<th># patients w/ scalp mets and no cooling</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spaeth</td>
<td>&lt;876</td>
<td>&lt;3 out of &lt;770</td>
<td>0 out of &lt;141</td>
</tr>
<tr>
<td>Protiere</td>
<td>214</td>
<td>0 out of 77</td>
<td>0 out of 137</td>
</tr>
<tr>
<td>Tollenar</td>
<td>35</td>
<td>0 out of 35</td>
<td>Uncontrolled</td>
</tr>
<tr>
<td>Ron</td>
<td>35</td>
<td>0 out of 19</td>
<td>0 out of 16</td>
</tr>
<tr>
<td>Middleton</td>
<td>24</td>
<td>0 out of 24</td>
<td>Uncontrolled</td>
</tr>
<tr>
<td>Lemeieux</td>
<td>640</td>
<td>6 out of 553 (1.1%)</td>
<td>1 out of 87 (1.2%)</td>
</tr>
</tbody>
</table>
UCSF “Hair To Stay” Program

• Completed
  – DigniCap pilot feasibility trial (UCSF and Wake Forest)

• Ongoing
  – Cold Cap Registry study
  – DigniCap pivotal trial for FDA submission

Funding for these programs has been generously provided by Ingrid Tauber and the Tauber Family Foundation
DigniCap™ Pilot Study

• Eligibility & Enrollment
  – Women with stage 1 breast cancer
  – 20 total = 16 at UCSF, 4 at Wake Forest

• Endpoints
  – Feasibility: < 50% pts discont. due to cap-associated toxicity.
  – Efficacy: ≤ grade 2 hair loss by the Dean’s scale.

DEANS SCALE
  Grade 0: no hair loss
  Grade 1: up to 25% hair loss
  Grade 2: between 25 and 50% hair loss
  Grade 3: between 50 and 75%
  Grade 4: greater than 75% hair loss
DigniCap™ Pilot Study

• **Eligibility & Enrollment**
  – Women with stage 1 breast cancer
  – 20 total = 16 at UCSF, 4 at Wake Forest

• **Endpoints**
  – Feasibility: < 50% pts discont. due to cap-associated toxicity.
  – Efficacy: ≤ grade 2 hair loss by the Dean’s scale.

• **Methods**
  – Independent Panel Assessment
  – Patient assessed
    – Toxicity
    – Hair loss
    – Quality of life & Body Image
    – Impact on treatment decisions
    – Hair re-growth
**DigniCap™ Pilot Study Results**

- **Feasibility**
  - 1 pt. stopped treatment (anxiety)

- **Toxicity**
  - All ≤ Grade 1 and 2
    - head/scalp pain
    - feeling chilled
    - rash

- **Quality of Life**
  85% of patients reported that the availability of scalp cooling made their decisions about chemotherapy easier.

### Hair Loss

<table>
<thead>
<tr>
<th>Grade</th>
<th>Independent Panel (%)</th>
<th>Patient (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 – 2</td>
<td>15 (75)</td>
<td>11 (55)</td>
</tr>
<tr>
<td></td>
<td>TC (n=16)</td>
<td>11</td>
</tr>
<tr>
<td></td>
<td>TCH (n=2)</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Nab (n=2)</td>
<td>2</td>
</tr>
<tr>
<td>3</td>
<td>2 (10)</td>
<td>3 (15)</td>
</tr>
<tr>
<td></td>
<td>TC</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>TCH</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Nab</td>
<td>-</td>
</tr>
<tr>
<td>4</td>
<td>3 (15)</td>
<td>6 (30)</td>
</tr>
<tr>
<td></td>
<td>TC</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>TCH</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Nab</td>
<td>-</td>
</tr>
</tbody>
</table>
DigniCap™ Pivotal Trial

• 110 patients at 5 centers (UCSF led)

• Completed accrual late Spring 2014

• FDA meeting October 2014
Penguin Cold Caps Registry opened in 2010.
  • Goal: Assess efficacy and tolerability in patients with early and advanced stage breast cancer.

Challenges to participation:
  • Financial investment
    – Avg. $2,500
  • Logistical support
    – Cold Cap Buddy
    – Freezer accessibility
  • Time Commitment
Methods for Evaluating Efficacy

Clinician Assessment:

**DEAN’S SCALE**

Grade 0: no hair loss
Grade 1: less than 25% hair loss
Grade 2: between 25 and 50% hair loss
Grade 3: between 50 and 75% hair loss
Grade 4: more than 75% hair loss

Patient Alopecia Self-Assessment

**VAS SCALE**

<table>
<thead>
<tr>
<th>0</th>
<th>10</th>
<th>20</th>
<th>30</th>
<th>40</th>
<th>50</th>
<th>60</th>
<th>70</th>
<th>80</th>
<th>90</th>
<th>100</th>
</tr>
</thead>
<tbody>
<tr>
<td>No hair loss</td>
<td>Half hair loss</td>
<td>Total hair loss</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Methods for Evaluating Tolerability

- Patient Symptoms Survey
  - Headaches during use of cold caps?
  - Cold during use of cold caps?
  - Satisfied with hair texture and quality?
71 Penguin Cold Cap participants

Women 29 to 67 years
  - Mean Age: 50 years

73% White Female
Chemotherapy Regimens

<table>
<thead>
<tr>
<th>Chemotherapy Regimens</th>
<th>(N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Docetaxel-Cytoxan x 4 cycles (TC x 4)</td>
<td>25</td>
</tr>
<tr>
<td>Paclitaxel, Doxorubicin-Cytoxan (T-AC)</td>
<td>23</td>
</tr>
<tr>
<td>Docetaxel-Cytoxan x 6 cycles (TC x 6)</td>
<td>11</td>
</tr>
<tr>
<td>Doxorubicin-Cytoxan, Paclitaxel (AC-T)</td>
<td>6</td>
</tr>
<tr>
<td>Eribulin or Abraxane</td>
<td>4</td>
</tr>
<tr>
<td>Paclitaxel</td>
<td>2</td>
</tr>
</tbody>
</table>

- Efficacy and tolerability of Penguin Cold Caps within TC x 4 cohort
Penguin Cold Caps with TC x 4: Is it Worth Taking the Plunge?

- Freeze Caps 24 hours
- Pre-Chemo Cooling 50 minutes
- Chemotherapy Infusion 120 – 180 minutes
- Post-Chemo Cooling Minimum of 120 min.

TC x 4: 25 patients
- Mean Age: 48 years
- 40% Post-Menopausal
- 76% White Female

Assessments at each cycle and post-chemo follow-up
25% average hair loss after 4 cycles
Greatest hair loss between cycles 1 and 2
100% reported no need to use wig
Patient and clinician assessments consistent
Headaches: Experienced by over 50% of patients
Amount of Chill: Quantified at 40 (on 100 pt. scale)
At Cycle 4, 78% reported satisfaction with the quantity, quality, and texture of their hair
Follow-Up: Satisfaction (TC x 4)

- 32% expressed some dissatisfaction with ease of use and convenience of Penguin Cold Caps

- 72% highly recommend Penguin Cold Caps to another patient
Conclusions (TC x 4)

- Using Penguin Cold Caps during TC x 4 may reduce Chemotherapy-Induced Alopecia to ~25%.

- Majority of Penguin Cold Cap users on TC x 4 have been very satisfied with the efficacy results.

- If a patient has adequate financial and logistical support, she should consider using Penguin Cold Caps for TC x 4.
Future Directions

- Publish data
- Advocate and seek FDA Approval Strategies
- Insurance authorization and reimbursement
- Broader patient access to knowledge of cooling options
- Test improvements in technology
- Advocacy
- Funding
A personal tale...

“I can't tell you how much keeping my hair allowed me to live a more "normal" life during and after treatment.”
THANK YOU!

A special thanks to...

- Penguin Cold Cap patients of the BCC!
- Hair 2 Stay Funding Team
  - Ingrid Tauber and the Lazlo Tauber Family Foundation
- Dr. Hope Rugo and Dr. Laura Esserman
- BCC Cold Cap Interns
  - Kate Serrurier
  - Alexa Glencer
  - Elizabeth Ver Hoeve
  - Brooke Rice
- UCSF Infusion Center Nurses and Staff
- Cancer Resource Center