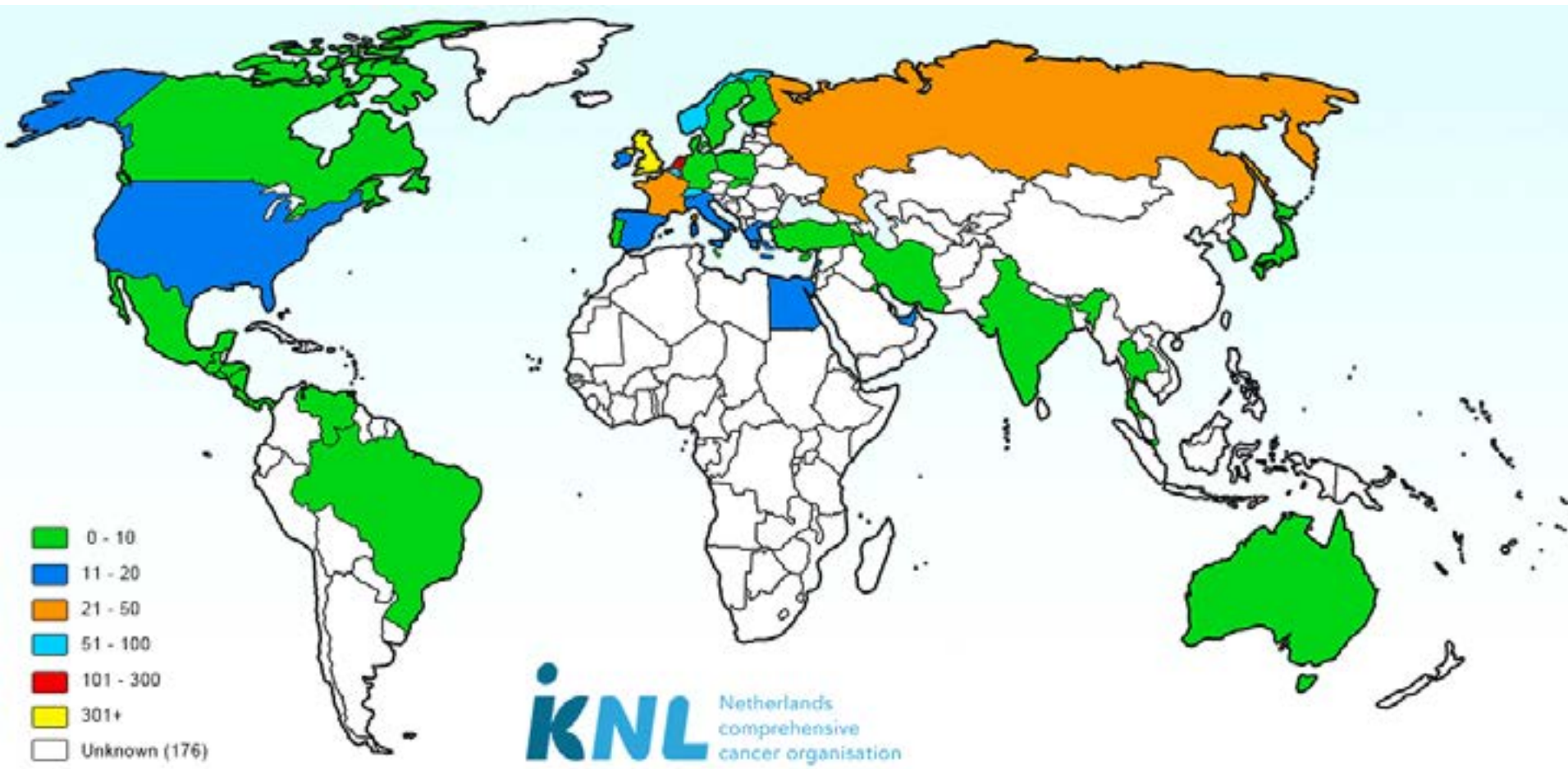
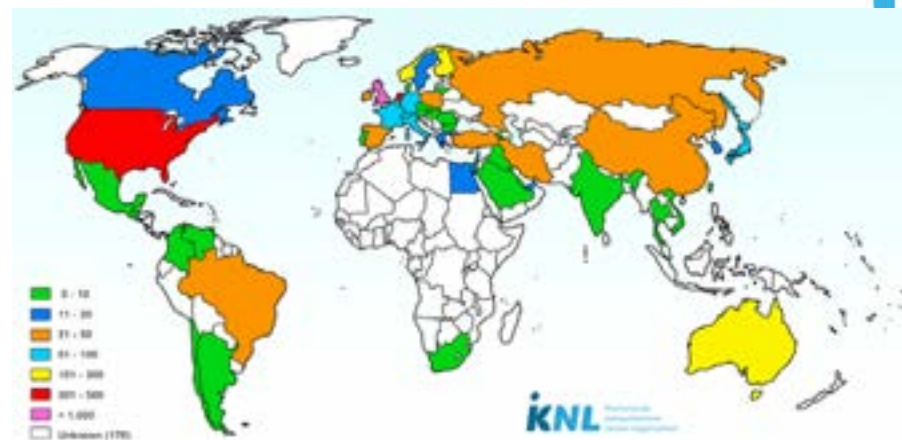


Scalp cooling worldwide

June 28 2018, Vienna, Corina van den Hurk

Scalp cooling machines world wide 2014





Rationale

- Incidence alopecia in solid tumors (Dutch Cancer Registry)
 - 24% of patients receive chemotherapy at primary diagnosis i.e. excl. follow up (recurrence/metastas)
 - 48% of chemo's cause severe alopecia
- Alopecia might introduce severe impact on Quality of Life

Table 4 Current preventive and therapeutic approaches for chemotherapy-induced alopecia (CIA)²¹⁻⁴⁸

Preventive approaches to reduce CIA		
Proven efficacy	No proven efficacy	Currently under investigation
<ul style="list-style-type: none"> • Scalp hypothermia "DigniCap" • "Paxman" 	<ul style="list-style-type: none"> • Topical calcitriol • Topical minoxidil (2% or 5%) • α-Tocopherol 	<ul style="list-style-type: none"> • Topical vasoconstrictors; Epinephrine • Norepinephrine • Cyclin-dependent kinase-2 • Interleukin-1 • p53 inhibitors • Epidermal growth factor • Fibroblast growth factor
Therapeutic approaches to speed regrowth after CIA		
<ul style="list-style-type: none"> • Topical minoxidil 2% • Bimatoprost ophthalmic solution 0.03% 		

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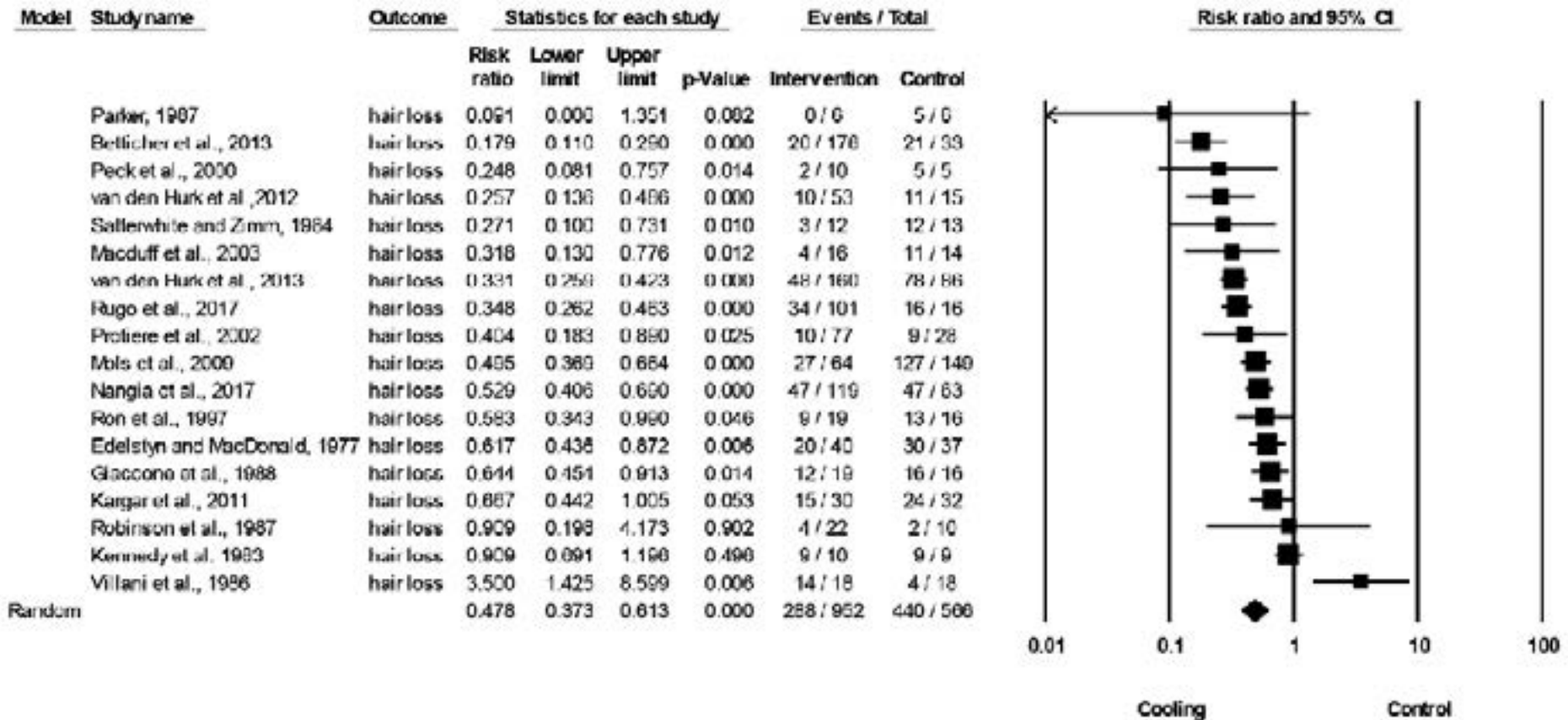
Literature: 95 full papers since 1979

- Efficacy: patient series
 - 8 RCTs
 - 4 including determinants in uni/multivariate analyses
- 15 reviews (from 2005)
- 7 safety/metastases
- 8 temperature
- 7 opinions/ QoL
- 2 Post-Infusion Cooling Time (PICT)
- 1 cost-effectiveness

Literature – RCTs

Study	SC (n=)	No SC (n=)	SC/ No SC % no wig or hc	p-value
1977 Edelstyn	40	37	50 / 19	<0.05
1983 Kennedy	10	9	10 / 0	NS
1984 Satterwhite	12	13	75 / 8	0.0009
1987 Parker	6	6	100 / 17	<0.01
1988 Giaccone	19	16	37 / 0	<0.025
1997 Ron	19	16	85 / 63	0.014
2003 Macduff	15	15	25 / 0	0.001-0.012
2017 Nangia	95	47	51 / 0	0.006

Literature – reviews Shah / Shin



$I^2 = 86.661$, $P < 0.001$

Figure 3 Effect of scalp cooling on hair loss by individual study.

Literature – review

n=17 observational with controls, 7 with statistics

Spaeth <i>et al.</i> (2008)	770	141	Multiple combinations	No head cover required	46% (31%)	p < 0.0018
Van den Hurk (2010)	160		Multiple combinations	No head cover required	(9%)	#
				Graded scale	(9%)	
Lemenager <i>et al.</i> (1997)	98		DT100	No head cover required	49%	#
				Graded scale	70%	
Belpomme <i>et al.</i> (1982)	72	77	Multiple combinations	No wig required	72% (38%)	2 out of 5 schedules p < 0.001
van den Hurk <i>et al.</i> (2010)	62	149	D60, C100; F500, E90, C500; DT75, D50, C500	Graded scales	52% (0%)	WHO: p < 0.001 VAS: p < 0.0001
Protiere <i>et al.</i> (2002)	27	109	Mi12, C600	Graded scale	41% (16%)	p < 0.05
Villani <i>et al.</i> (1986)	18	18	Combinations including D	Graded scale	67% (17%)	Significant

n=36 observational without controls: 80% good result

Literature – patient series

Table II. Head cover use during the last scalp cooling session according to type of chemotherapy.

Chemotherapy and planned dosage (mgr/m ²) ^a	No head cover/total (%)
A60C600 (AC)	29/74 (39)
A60C600/D100 ^b (ACD)	10/16 (63)
ACT Overall	20/50 (40)
A60C600/T80 ^b (ACT80)	14/29 (48)
A60C600/T175 ^b (ACT175)	6/21 (29)
D75A50C500 (TAC)	5/66 (8)
D Overall ^f	87/120 (73)
D75	31/33 (94)
D100	27/44 (61)
D75combi ^c	21/33 (64)
F500A50C500 (FAC)	21/39 (54)
FEC Overall ^f	371/752 (56)
F500E50-70C500 (FE50-70C)	22/38 (58)
F500/600E75-85C500/600 (FE75-85C)	16/32 (50)
F500E90C500 (FE90C)	292/558 (52)
F500/600E100C500/600 (FE100C)	40/123 (33)
F500E100C500/D100 ^b (FE100CD)	22/46 (48)
TCarbo Overall ^f	31/68 (46)
T70-100Carbo	9/12 (75)
T175Carbo	20/52 (38)
T70-90	34/42 (81)
Irino350	12/42 (29)
Other ^c	49/64 (77)
Total	709/1411 (50)

Literature – temperature math model

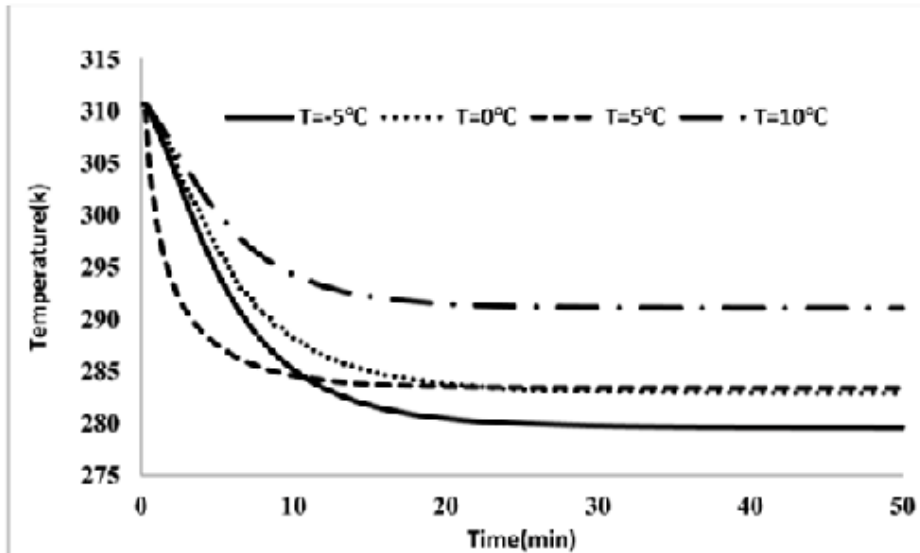


Figure 8: Mean temperature distribution inside the scalp skin for different coolant temperature during the cooling process.

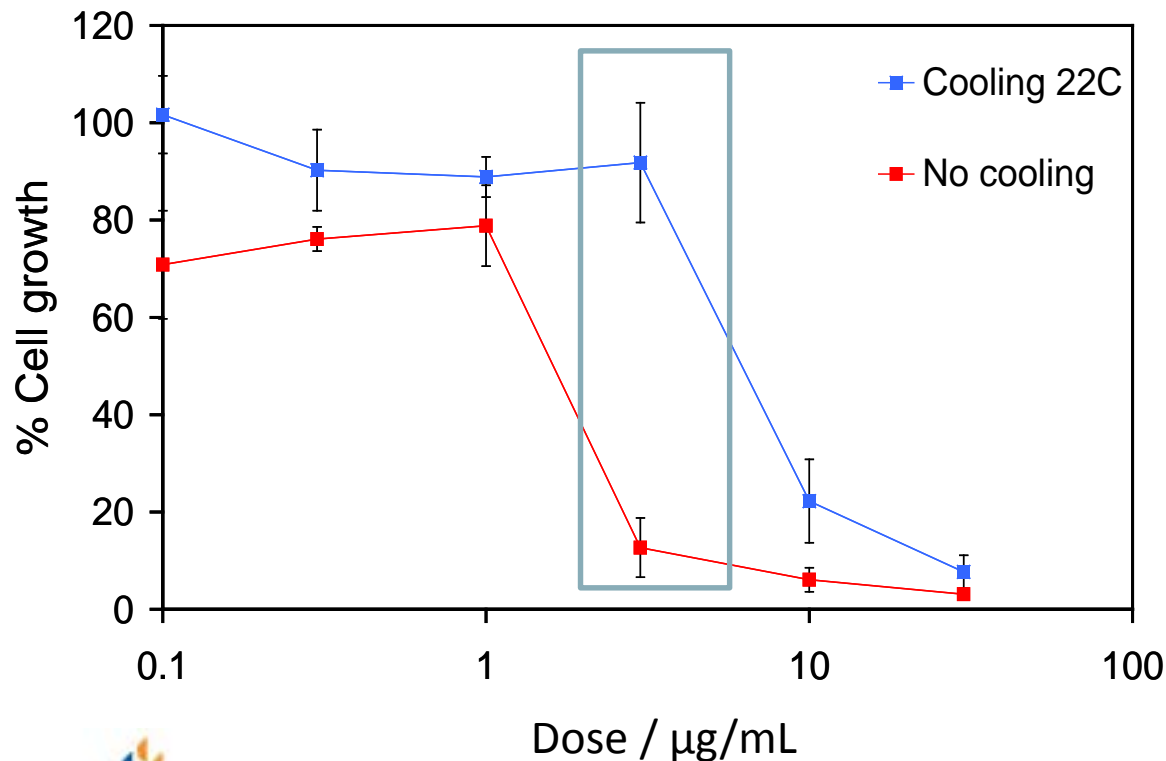
- Heat extraction
- Perfusion
- Temp tissue depends
 - Temp coolant
 - Thermal resistance hair/air

Coolant temperature (°C)	Min. scalp temperature (°C)	Perfusion decrease
-5	6.4	10%
5	10.22	13%
10	17.68	21%

Table 4: Effect of changes in coolant temperature on minimum scalp temperature (T_{skin}) and relative perfusion during cooling.

Literature – temperature in vitro

Normal Human Epidermal Keratinocytes treated with
“Drug X” (0.1-30 μ g/mL) at different temperatures (22°C and 37°C)



Literature – temperature sensor

Komen:

- Breast cancer, n= 62
- Coolant -4°C, mean scalp skin temperature 19°C (10 - 31°C)
- Temperature <18°C= better result, but inconclusive

Ekwall:

- Ovarian/ endometrial cancer
- 3°C (n=5) skin temp <22°C
- 3 vs 8 °C (n=43):
difference VAS but not CIA
- K&E -> CIA less after cyle 2

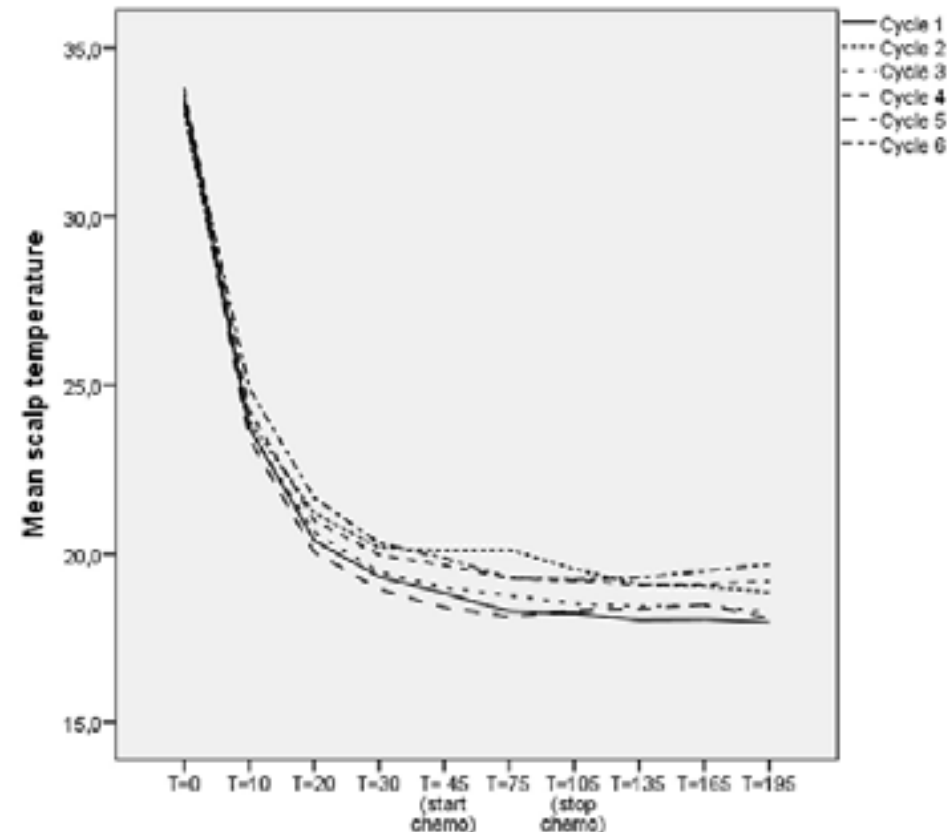


Fig. 1. Mean scalp skin temperatures in degrees Celsius on repeated measurement in all patients during scalp cooling during 6 cycles of anthracycline-containing chemotherapy.

Literature - PICT

Docetaxel 3-weekly; 75 / 100 mg/m²

Table 2 Use of wig or head cover in scalp-cooled patients with different PICTs

	PICT (min)	<i>n</i>	% no wig or head cover
Observational	90	53	81
Randomised	90	38	79*
	45	38	95*

**p*=0.04 (90 vs 45 min)

	20-min post-infusion cooling time (<i>n</i> = 64)	45-min post-infusion cooling time (<i>n</i> = 70)	<i>P</i> value
Evaluable for scalp cooling	45	52	0.5
Patients with head covering	12/45 (27 %)	11/52 (21 %)	
Patients without head covering	33/45 (73 %)	41/52 (79 %)	

Literature - determinants

H&S&F:

- Type and dose of chemotherapy
- Age: older= ↓

Multivariate, n=1411

Infusion time: shorter = ↓
Type of hair determined
by race: African/Asian= ↓

Univariate, n=226

Comorbidity= ↓
Neutropenia= ↓
Smoking= ↓
Hair density: higher= ↓

Rugo: no differences in age, hair thickness, hormonal therapy
and BMI

Literature - regrowth

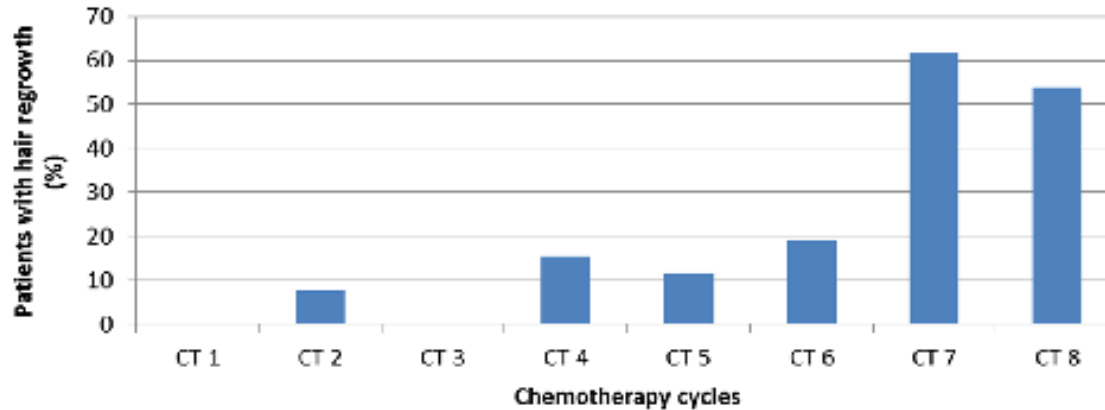


Figure 1 Percentages of patients with hair regrowth (n = 20) in breast cancer patients under EC/Doc (n = 26). The observed regrowth is shown due to specific CT-cycle.

Hurk

- During chemo 24% SC (n=160) vs 7% non-SC (n=86)

Literature - regrowth



Figure 1 On the left, grade 2 alopecia after four cycles of docetaxel, carboplatin, and trastuzumab, before starting scalp cooling. On the right, hair regrowth after 5th cycle with scalp cooling and topical minoxidil 5%.

Conclusion

- Protection from further damage of follicles
- Prevention of persistent alopecia?

Next steps

Focus for research:

1. PICT
2. Improve results
 - PICT
 - Temperature
 - Pharmacokinetics
 - Topicals



-> Increase availability of scalp cooling world wide



www.scalpcooling.org



c.vandenhurk@iknl.nl



twitter.com/iknl