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Testing commercially available topical skin care products for their effect on Tumor Treating Fields (TTFields) therapy array adhesiveness and electric currents delivery

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Introduction

- Tumor Treating Fields (TTFields) are electric fields that disrupt cellular processes critical for cancer cell viability and tumor progression.[1]
- TTFields therapy is approved for the treatment of recurrent glioblastoma (GBM), newly diagnosed GBM, pleural mesothelioma, and non-small cell lung carcinoma (NSCLC), and is currently under clinical investigations for the treatment of other types of solid tumors.[2-3]
- TTFields therapy is delivered continuously and non-invasively, using a portable signal generator connected to 4 arrays attached to the skin surrounding the tumor region, adhering to the body through a thin layer of conductive medical gel.[2]
- The main treatment-related adverse effect (AEs) reported in clinical studies and post-marketing surveillance studies has been low-grade skin irritation under the arrays,[4-5] which may be treated in most cases with the use of topical skin care products or intermittent treatment interruptions.[6-7]
- Treatment of such skin irritation is important for improving patient's quality of life. Additionally, appropriate skin care will allow increasing device usage, shown to directly elevate treatment effectiveness. [8]
- TTFields application may cause heating under the arrays, hence the device is designed to reduce the electrical current when needed to prevent overheating. As treatment effectiveness depends on field intensity,[8] topical products that introduce high resistance to the array-skin interface may cause temperature elevation, resulting in reduced currents and impaired treatment effectiveness.

Aim

To examine the effects of commercially available skin care products on array adhesiveness and electric current delivery.

Conclusions

- This study identified, under controlled conditions, a selection of commercially available skin care products that do not compromise TTFields delivery and hence may serve as candidates for managing skin AEs in TTFields-treated patients.
- The concordance between the clinical and preclinical results confirms the use of the high throughput preclinical approach.
- When skin AEs occur, they should be managed to prevent exacerbation to more severe forms of skin AEs, using topical skin care products carefully selected so they will not compromise TTFields delivery.
- Implementing proactive measures for skin care are necessary to maintain patient quality-of-life and increase device usage for better treatment effectiveness.

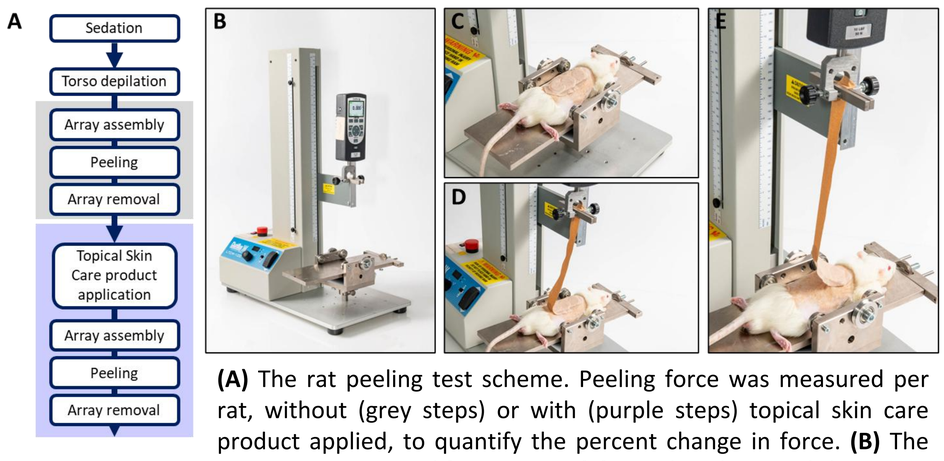
References: 1. Karanam, N. K. and M. D. Story (2021). Int J Radiat Biol 97(8): 1044-1054. 2. Mun, E. J., et al. (2018). Clin Cancer Res 24(2): 266-275. 3. Leal, T., et al. (2023). Lancet Oncol 24(9): 1002-1017. 4. Shi, W., et al. (2020). J Neurooncol 148(3): 489-500. 5. Vergote, I., et al. (2019). Inter J Rad Oncol Biol Physics 105(1): E587. 6. Lacouture, M. E., et al. (2014). Semin Oncol 41 Suppl 4: S1-14. 7. Anadkat, M. J., et al. (2022). Front Oncol 12: 975473. 8. Ballo, M. T., et al. (2023). J Neurooncol 164(1): 1-9.

Abbreviations: AE, adverse effects, BMI, body mass index; INE, insulated electrode; Max, maximum; Min, minimum; NA, not assessed; SD, standard deviation.

Results

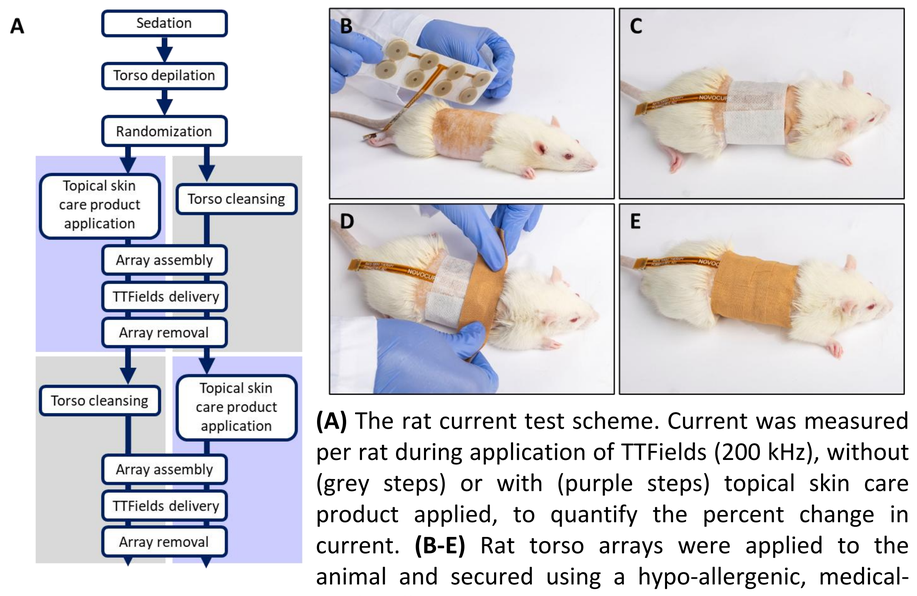
FIGURE 1. Testing the effect of topical skin care products on array adhesiveness and electric currents delivery in rats.

Mechanical Functionality Testing of Topical Skin Care Products in Rats



(A) The rat peeling test scheme. Peeling force was measured per rat, without (grey steps) or with (purple steps) topical skin care product applied, to quantify the percent change in force. **(B)** The LTCM-100 motorized force tester. **(C)** Rat placed on its abdomen on the moving platform of the force tester and the array part applied to its back. **(D)** An adhesive strip connected to the dorsal edge of the array and to the machine's motorized arm. **(E)** The machine arm pulling the array from the rat back.

Electrical Functionality Testing of Topical Skin Care Products in Rats



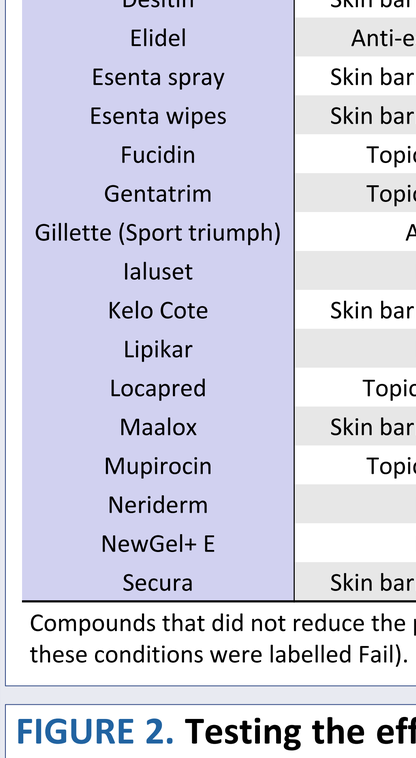
(A) The rat current test scheme. Current was measured per rat during application of TTFields (200 kHz), without (grey steps) or with (purple steps) topical skin care product applied, to quantify the percent change in current. **(B-E)** Rat torso arrays were applied to the animal and secured using a hypo-allergenic, medical-grade adhesive.

Force and Current Change for the Topical Skin Care Products Tested on Rats

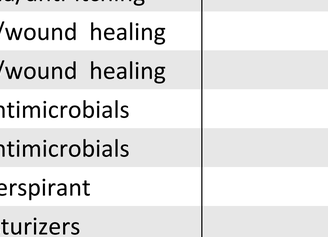
Topical Product	Medical Use	Application Method	Force Change (%)	Current		Pass/Fail
				Mean % Change ± SD	p-value	
Atoderm	Moisturizers	Cream	−5	−5.94 ± 4.79	0.082	Pass
Baby Pasta	Skin barriers/wound healing	Ointment	−63.2	NA	NA	Fail
Bepanthen Plus	Topical antimicrobials	Cream	−79.9	NA	NA	Fail
Betacortene	Topical corticosteroids	Cream	38.9	1.79 ± 12.17	0.841	Pass
Calamine	Anti-eczema/anti-itching	Suspension	109.9	−4.43 ± 3.92	0.106	Pass
Calendula	Skin barriers/wound healing	Cream	−100	NA	NA	Fail
Cavilon	Skin barriers/wound healing	Spray	341	1.29 ± 8.52	0.801	Pass
CeraVe	Moisturizers	Cream	43.2	−0.04 ± 14.77	0.882	Pass
Cicalfate	Skin barriers/wound healing	Cream	−30.7	−22.72 ± 7.33	0.009	Fail
Cicaplast	Skin barriers/wound healing	Cream	−100	NA	NA	Fail
Dermalibour+	Moisturizers	Foaming gel	48.2	8.13 ± 11.86	0.266	Pass
Dermovate	Topical corticosteroids	Cream	226.7	−1.88 ± 11.78	0.743	Pass
Desitin	Skin barriers/wound healing	Ointment	−38.9	−48.90 ± 4.85	0.0005	Fail
Elidel	Anti-eczema/anti-itching	Cream	83.3	2.24 ± 8.10	0.719	Pass
Esenta spray	Skin barriers/wound healing	Spray	78.6	−2.92 ± 10.63	0.568	Pass
Esenta wipes	Skin barriers/wound healing	Wipes	204.7	−0.50 ± 3.48	0.701	Pass
Fucidin	Topical antimicrobials	Cream	−61.5	NA	NA	Fail
Gentatrim	Topical antimicrobials	Cream	4.9	4.30 ± 4.71	0.1608	Pass
Gillette (Sport triumph)	Antiperspirant	Gel	−77.1	NA	NA	Fail
Ialuset	Moisturizers	Cream	77.1	−0.64 ± 8.37	0.85	Pass
Kelo Cote	Skin barriers/wound healing	Spray	−31.8	−27.31 ± 12.31	0.011	Fail
Lipikar	Moisturizers	Cream	4	0.98 ± 4.09	0.695	Pass
Locapred	Topical corticosteroids	Cream	1.9	0.79 ± 5.20	0.777	Pass
Maalox	Skin barriers/wound healing	Cream	−49.1	NA	NA	Fail
Mupirocin	Topical antimicrobials	Ointment	−13.5	3.72 ± 5.17	0.242	Pass
Neriderm	Moisturizers	Cream	−32.7	−17.99 ± 5.80	0.013	Pass
NewGel+ E	Moisturizers	Gel	−66.3	NA	NA	Fail
Secura	Skin barriers/wound healing	Spray	176.4	−4.65 ± 5.92	0.21	Pass

Compounds that did not reduce the peeling force by more than 40% and did not significantly reduce the electrical current were labelled Pass. Compounds that did not comply with these conditions were labelled Fail).

FIGURE 2. Testing the effect of topical skin care products on electric currents delivery in humans. We selected 8 compounds that passed the mechanical functionality test for examination in humans: 7 that did not significantly reduce the current in rat tests (Calamine, SensiCare, Dermovate, Secura, CeraVe, Esenta wipes, and Xeracalm), and 1 as a negative control (Staquis). The topical products that did not compromise array adherence nor significantly reduce the currents in the animal studies, did not compromise array adherence nor significantly reduced electrical currents in the human studies.



Array Placement on the Thighs During the Clinical Study



Investigational Topical Skin Care Product Disposition

Topical Product	Male, N (%)	Female, N (%)	All, N (%)
Calamine	0 (0)	7 (100)	7 (100)
CeraVe	4 (50.0)	4 (50.0)	8 (100)
Dermovate	0 (0)	7 (100)	7 (100)
Esenta wipes	6 (85.7)	1 (14.3)	7 (100)
Secura	5 (71.4)	2 (28.6)	7 (100)
SensiCare	4 (57.1)	3 (42.9)	7 (100)
Xeracalm	3 (42.9)	4 (57.1)	7 (100)
Total tests	22 (44.0)	28 (56.0)	50 (100)

Subjects' Baseline Characteristics

Covariate	Sex	Mean	SD	Min	Median	Max	N
Age (years)	All	36.3	10.3	20.0	36.5	59.0	26
	Male	36.0	11.0	23.0	33.5	59.0	12
	Female	36.5	10.0	20.0	38.5	51.0	14
BMI (kg/m^2)	All	25.9	5.8	17.0	24.8	44.0	26
	Male	26.4	3.7	21.6	25.5	33.4	12
	Female	25.5	7.3	17.0	23.1	44.0	14