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Red Deer Umbilical Cord Lining Mesenchymal Stem Cell Conditioned Media after Monopolar Radiofrequency Facial Treatment – A Case Series

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Abstract

Background: Monopolar radiofrequency (MRF) is a valuable non-ablative modality to treat mild-to-moderate skin laxity and wrinkles. As maximum MRF results are only achieved months after treatment, there is ongoing interest in enhancing efficacy.

Objective: To assess the effect of a serum containing Red Deer Umbilical Cord Lining Mesenchymal Stem Cell conditioned media (RD-CLMSC-CM) on skin rejuvenation outcomes after MRF.

Methods: Ten adults (30-64 years) with a clinical need for a facelift, based on the presence of mild to severe facial wrinkles, were treated with MRF. Afterwards, moisturizer was applied to the entire face. RD-CLMSC-CM was applied to the right half of the face, twice daily (morning and evening) for four weeks. QuantifiCare analysis was performed at baseline and 2, 4, 6, and 8 weeks.

Results: The difference between the intervention side and the control side was minimal at week 2. By week 4, however, the mean difference reached statistical significance ($p = 0.004$), which persisted through week 6 ($p = 0.021$) and week 8 ($p = 0.019$), consistently favoring the intervention side. On the intervention side, facial lifting improved significantly at weeks 4, 6 and 8, compared to week 2, while the control side did not show a significant improvement between week 2 and week 4.

Conclusions: This case series suggests that MRF combined with RD-CLMSC-CM serum may provide favorable clinical outcomes. These findings provide support for setting up randomized, controlled clinical trials to better assess the efficacy of RD-CLMSC-CM.

Keywords: Calecim, Mesenchymal stem cells, MSC-CM, MSC-derived conditioned media, Stem cells, Monopolar radiofrequency, Skin tightening

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Introduction

Facial wrinkles are a common indicator of ageing, often prompting individuals to seek cosmetic treatments to restore a youthful appearance. Monopolar radiofrequency (MRF) is a valuable non-ablative modality to treat early, mild-to-moderate skin laxity and wrinkles, particularly in the lower face and neck, but without the post-treatment downtime and risks of serious side effects and complications associated with more invasive procedures [1-3]. The technique uses a single active electrode to generate controlled heat in the dermal layers, stimulating collagen and elastin production, promoting tissue contraction, and gradually improving skin texture, tightness, and tone [2,4,5].

Although MRF treatment results in immediate skin tightening, maximum results are only achieved months after treatment; thus, there is ongoing interest in enhancing the efficacy of this treatment [3]. Advances in regenerative medicine have highlighted the potential of stem cell-based therapies, such as cord lining mesenchymal stem cells (CLMSCs)-derived conditioned media (CM), for cosmetic applications to improve tissue repair and rejuvenation [6]. Red Deer Umbilical Cord Lining Mesenchymal Stem Cell conditioned media (RD-CLMSC-CM) is particularly interesting due to its high concentration of growth factors, cytokines, and extracellular matrix proteins that address intrinsic factors of skin aging, such as the decline in collagen, hyaluronic acid, and elastin levels [7-9].

While previous studies have demonstrated the effectiveness of combining stem cell-based serums with ablative rejuvenation treatments [8,10], the potential of stem cell therapy as an adjunct to non-ablative treatments like MRF has not been explored. This study aims to assess the effect of

a serum containing RD-CLMSC-CM on skin rejuvenation outcomes after MRF treatment.

Materials and Methods

Study design

The study was a prospective, single-center, split-face case series conducted between March 2024 and May 2024 with patients who underwent full-face, MRF treatment at the privately owned Demis Clinic in Bangkok, Thailand. This case series study has been reported in line with the PROCESS 2020 Guideline [11].

Participants

The participants enrolled in this study were adults of any gender, aged between 20 and 70 years, who demonstrated a clinical need for a facelift. Eligibility was determined based on the presence of mild to severe facial wrinkles, as assessed by the Fitzpatrick-Goodman Classification of Wrinkling and Degree of Elastosis Scale (Table 1) [8,12]. Participants were required to attend a single treatment session and commit to follow-up visits at weeks 2, 4, 6, and 8.

Participants were excluded from the study if they had received other lifting treatments within the six months before study initiation or had filler or Botox injections at the treatment sites within the two months before the study. Additional exclusion criteria included the use of oral or topical steroids within one month before the study due to their impact on the skin's inflammatory response to laser treatment. Participants were also excluded if they had skin diseases such as skin cancer, warts, solar keratoses, acne, open wounds, or facial infections like herpes or impetigo in the targeted treatment area. The use of oral vitamin A derivatives within six months before the study, a history of allergic reactions to stem cell-derived growth factors, the presence of a pacemaker, and pregnancy or breastfeeding were also grounds for exclusion.

Participants were subject to withdrawal from the study under several conditions. These included experiencing severe side effects from the application of stem cell-derived growth factors, such as skin infections. Additionally, participants who failed to adhere to the study requirements or could not attend follow-up appointments as scheduled were also subject to discontinuation. Withdrawal could also occur upon the participant's voluntary request to leave the study or if the participant became pregnant during the study period.

Pre-Intervention patient optimization

Before the intervention, researchers collected a general history, including the participant's first and last name, age, gender, address, and telephone number. They also documented any history of drug allergies, underlying diseases, and the use of oral or topical medications, as well as any history of drug allergies and wound healing. A general physical examination and a detailed examination of the skin was conducted. For female participants, additional information on menstruation, pregnancy, and breastfeeding was gathered, and a urine pregnancy test was administered to confirm the absence of pregnancy.

Treatment

Red Deer Umbilical Cord Lining Mesenchymal Stem Cell - Conditioned Media (RD-CLMSC-CM) Serum was of the brand CALECIM® Professional Serum (CALECIM Cosmeceuticals, Singapore). The serum contained 50% v/v conditioned media derived from RD-CLMSC cultures, integrated into the proprietary transdermal complex PTT-6® (Stem cell-derived Fibronectins, Glycoproteins, Albumin, Collagens, Hyaluronic Acid) to allow the penetration of protein growth factors into the epidermis [7,13].

Treatment protocol

Before radiofrequency treatment, the participant's faces were cleaned with mild soap, wiped with an antimicrobial solution (chlorhexidine gluconate) and left to dry. They then received MRF treatment with 125-600 shots of energy to the entire face, using the "VolNewMer" (VNM: Classys, Seoul, Korea) device with 4 cm^2 V-tips. The RF energy intensity from the high-frequency equipment was set to a maximum level of 5, 115 J, 28.75 J per cm^2.

Following the MRF treatment, a moisturizer (Physiogel® Soothing Care A.I. lotion) was applied to the entire face (approximately one fingertip unit ≈ 0.5g). The moisturizer was followed by CALECIM® Professional Serum, which was applied 1-2 drops at a time and only to the right half of the face. Participants were directed to apply the serum twice daily (morning and evening) for four weeks. Approximately two bottles of serum were used per participant. After applying the serum in the morning, participants were advised to apply sunscreen (SPF 50+ PA index +++) daily to the entire face. During the study, participants could apply makeup as usual but were advised against using facial masks, scrubs, or creams containing whitening ingredients such as extracts of vitamin C and vitamin A or weak acids/ skin exfoliants such as Alpha Hydroxy Acid (AHA) or Beta Hydroxy Acid (BHA).

Clinical assessments

During the study, the participants' facial photographs were taken using a high-resolution Fujifilm digital camera on their left at (45° and 90°) and right at (-45° and -90°). Photographs were taken before initial treatment with CALECIM® Professional Serum (Week 0) and at follow-up visits at Weeks 2, 4, 6, and 8.

Participant results were also assessed using the QuantifiCare 3D imaging system (QuantifiCare, USA) for measuring skin lifting [14]. QuantifiCare analysis was performed at baseline and 2, 4, 6, and 8 weeks after the start of the CALECIM® Professional Serum regimen.

Patient Self-assessment

Participants analyzed the treatment results subjectively by evaluating paired photographs before and 8 weeks after the treatment. Participants made subjective clinical assessments of skin lifting and tightening by evaluating their own photos. Subjective improvement was evaluated using the Global Aesthetic Improvement Assessment (GAIS): 'worse' (1), 'no change' (2), 'improved' (3), 'much improved' (4), and 'very much improved' (5) [15].

Statistical analysis

Data analysis was performed using the Stata version 17.0. Continuous data were presented as mean and standard deviation (SD), and a pre-t-test and repeated ANOVA test were used to test the difference in the quantitative data. A P-value of less than 0.05 was considered significant.

Results

Participant characteristics

The study included ten female participants, with a mean age of 40.6 years, ranging from 30 to 64 years. The participants had Fitzpatrick skin types III and IV, with mild to moderate facial wrinkles (Table 2). All ten participants completed the treatment and follow-up sessions. No adverse events were noted during or after treatment by the participants or the investigator.

Table 1: Fitzpatrick-Goldman classification of wrinkling and degree of elastosis scale.

Class	Wrinkling	Score	Degree of Elastosis
I	Fine wrinkles	1–3	Mild (fine textural changes with subtly accentuated skin lines)
II	Fine to moderate-depth wrinkles, moderate number of lines	4–6	Moderate (distinct popular elastosis [individual papules with yellow translucency under direct lighting] and dyschromia)
III	Fine to deep wrinkles, numerous lines, with or without redundant skin folds	7–9	Severe (multi-papular and confluent elastosis [thickened yellow and pallid] approaching or consistent with cutis rhomboidalis)

Adapted from E. Hoss et al., J Drugs Dermatol. Nov 1, 2020;19(11):1044-1048 [8].

Table 2: Patient Characteristics.

Characteristics		Value (N = 10)
Sex	Female	10 (100%)
	Male	0 (0%)
Age, mean; SD (range)		40.6, 9.45 (30-64)
FiitzPatrick Skin Type	Type III	4 (40%
	Type IV	6 (60%)
Wrinkling/elastosis*	Mild (Class I)	9 (90%)
	Moderate (Class II)	1 (10%)

* FitzPatrick-Goldman Wrinkling and Degree of Elastosis Score

Table 3: Clinical improvement.

Weeks	n	Right (Rt)	Left (Lt)	Mean difference (95%CI)	p-value
		Mean ± SD.	Mean ± SD.		
2 weeks	10	2.07 ± 0.61	1.85 ± 0.46	0.22 (-0.08, 0.51)	0.129
4 weeks	10	2.92 ± 1.38	2.37 ± 1.17	0.55 (0.23, 0.88)	0.004*
6 weeks	10	3.72 ± 1.84	3.16 ± 1.55	0.56 (0.11, 1.02)	0.021*
8 weeks	10	4.08 ± 1.74	3.51 ± 1.65	0.57 (0.12, 1.02)	0.019*

Paired t-test, * indicates a statistically significant difference (p<0.05)

Investigator-assessed clinical improvements

The QuantifiCare SkinCare assessments over the 8-week period demonstrated progressive improvements in facial lifting on both sides of the face from baseline. However, the clinical improvements were more pronounced overall on the right side, which received the RD-CLMSC-CM serum treatment plus moisturizer, compared to the moisturizer-only treated side (left). As shown in Table 3 and Figure 1, the difference between the sides was minimal and not statistically significant at week 2. By week 4, however, the mean difference had increased to 0.55, reaching statistical significance (p = 0.004). This significant difference persisted through week 6 (mean difference: 0.56, p = 0.021) and week 8 (mean difference: 0.57, p = 0.019), consistently favoring the right side. Clinical images provided in supplementary figure S1 (Cases 1-3) further illustrate these differences, highlighting the visible improvements on the right side over time.

Table 4 and Supplemental Figures S2a-c compare the difference in facial lifting scores observed between the RD-CLMSC-CM serum-treated sides (right) and moisturizer-only sides (left) over various time points. On the right side, there were statistically significant improvements in facial lifting at all measured intervals compared to week 2. In contrast, the left side did not show a statistically significant difference between week 2 and week 4. However, significant improvements were observed at weeks 6 and 8 on the left side.

Patient self-assessment

Subjectively, on the right side, 10% (n=1) of participants reported 'very much improved', and 90% (n=9) of participants reported 'much improved'. On the left side, 70% (n=7) of participants reported 'much improved' and 30% (n=3) of participants reported 'improved'. Finally, 30% (n=3) of participants reported that the right side improved more than the left side, and most participants felt satisfied with the results on both sides.

Table 4: Comparison of difference scores in facial lifting between each side.

Right			Left	
Weeks	Mean difference (95%CI)	*p-value*	Mean difference (95%CI)	*p-value*
2 vs. 4	0.85 (0.19, 1.51)	0.017*	0.51 (-0.21, 1.24)	0.143
2 vs. 6	1.65 (0.59, 2.71)	0.007*	1.31 (0.27, 2.34)	0.019*
2 vs. 8	2.01 (0.98, 3.04)	0.002*	1.66 (0.52, 2.79)	0.009*

Repeated ANOVA test, * = significant difference

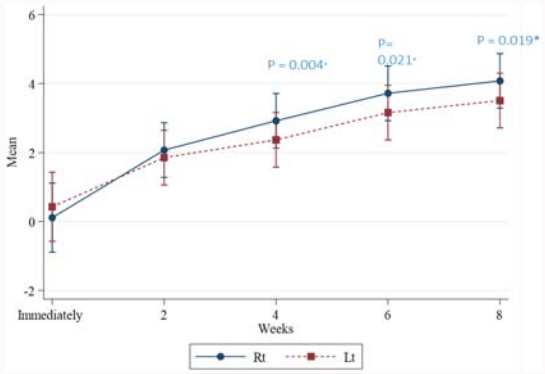

Figure 1: Clinical improvement.
* = significant difference

All 10 participants completed treatment and follow-up examinations without serious side effects.

Discussion

Since its approval by the Food and Drug Administration in 2002 for wrinkle treatment and in 2004 for full-face skin tightening, MRF has gained recognition as an effective non-surgical procedure [3,16]. Moreover, unlike other energy-based modalities, MRF is not significantly affected by tissue diffraction or absorption by epidermal melanin, making it suitable for all skin types [3].

Most non-invasive skin rejuvenation procedures aim to trigger a wound repair response, encouraging the body to replenish or remodel old or damaged tissues [4]. In RF therapy, the controlled thermal damage induces immediate collagen contraction and stimulates ongoing collagen production and remodeling [3,5]. This process mimics wound healing, with collagen remodeling beginning after an increase in type I collagen mRNA expression [16]. The resulting increase in collagen fibers leads to gradual skin tightening, with optimal results typically seen 4 to 6 months post-treatment and lasting up to 1 year [5,16].

The structural integrity of the skin largely depends on fibroblasts, which synthesize elastin and collagen proteins [17]. Elastin proteins ensure the skin's elasticity, while collagen fibers contribute to resilience and tensile strength. The human dermis is primarily composed of

type I collagen, which consists of three polypeptide chains stabilized through a triple-helix structure formed by cross-linking. However, ageing is accompanied by a decline in these key proteins, along with reduced collagen cross-linking stability and increased oxidative stress and matrix metalloproteinase activity, which together contribute to the development of wrinkles and loss of skin elasticity [16,17].

Mesenchymal stem cells (MSCs), particularly those derived from umbilical cord blood and umbilical cord lining, show great promise in addressing skin ageing by boosting collagen and elastin production [7-9,17]. MSCs are known for their rapid proliferation and ability to secrete growth factors such as EGF, TGF-β, PDGF, and GDF-11, which support skin regeneration and collagen type I synthesis [18]. Studies using cord blood and cord lining-MSC-conditioned mediums have shown an increase in the presence of elastic fibers and restructuring of the collagen matrix within the dermis, leading to significant improvements in skin density and wrinkle reduction, thus highlighting their potential as an effective anti-ageing therapy [17,18].

While promising findings exist regarding the use of RD-CLMSC-CM in facial rejuvenation, particularly with ablative resurfacing [8], direct studies on its combination with non-ablative techniques have not yet been conducted. To the best of the authors' knowledge, this is the first study in which an RD-CLMSC-CM topical serum is used alongside MRF therapy to treat mild to moderate facial wrinkles. In this split-face case series, facial lifting was significantly enhanced on the right side (intervention) at all time points, while on the left side (comparator), significant improvements were evident starting from week 6. This suggests that the use of RD-CLMSC-CM accelerates facial lifting after MRF therapy.

In summary, this case series suggests that a single session of MRF combined with RD-CLMSC-CM serum may provide favorable clinical outcomes. These findings, although based on a small sample size and short follow-up duration, provide support for setting up randomized, controlled clinical trials to better assess the efficacy of RD-CLMSC-CM as an adjunct therapy for MRF.

Supplementary Materials

The following supporting information is supplied, Figure S1: Clinical images: Pre-intervention & Peri-Intervention; Figure S2: Comparison of difference scores in facial lifting.

Author Contributions

DP conceptualized the study, and DP, PB, and PA conducted the research and did the formal analysis and data visualization. DP wrote the original draft, and PB and PA reviewed and edited. All authors approved the final version for submission.

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Informed Consent Statement

Having had the study protocol explained to them, including potential side effects, all participants gave written informed consent to participate in this study and for the use of their clinical photography.

Data Availability Statement: Data can be obtained from the corresponding author upon reasonable request.

Conflicts of Interest: The authors declare that the manuscript preparation was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

DP has served as a speaker for speaking events and medical education for A. Menarini (Thailand) Ltd. Results of this study have been presented by DP in seminars/meetings as a part of the Menarini Medical Education Program.

References

1. Wanitphakdeedecha R, Yogya Y, Yan C, Phumariyapong P, Nanchaipruek Y, Thongjaroensirikul P, et al. Efficacy and Safety of Monopolar Radiofrequency for Treatment of Lower Facial Laxity in Asians. Dermatol Ther (Heidelb). 2022;12(11):2563-73.
2. Shin J, Sung Y, Jin S, Hwang C-L, Kim H, Hong D, et al. Efficacy and Safety of Monopolar Radiofrequency for Tightening the Skin of Aged Faces. Cosmetics. 2024;11(3):71.
3. El-Domyati M, El-Ammawi TS, Medhat W, Moawad O, Brennan D, Mahoney MG, et al. Radiofrequency facial rejuvenation: Evidence-based effect. J Am Acad Dermatol. 2011;64(3):524-35.
4. Kilmer SL, Lupo MP, Marmur E, Dyke S. Consensus recommendations for 4th generation non-microneedling monopolar radiofrequency for skin tightening: a Delphi consensus panel. J Drugs Dermatol. 2020;19(1):20-6.
5. Hwang Y, Arayaskul S, Vachiramon V, Yi KH. Subjective evaluation of monopolar radiofrequency treatment by patients in aesthetic rejuvenation. Skin Res Technol. 2024;30(2):e13593.
6. Shimizu Y, Ntege EH, Sunami H. Current regenerative medicine-based approaches for skin regeneration: A review of literature and a report on clinical applications in Japan. Regen Ther. 2022;21:73-80.
7. Ong C, Lim I, Goldman M, Hartman N, Masilamani J, Phan T. Improvement in Skin Elasticity Using Red Deer Umbilical Cord Lining Mesenchymal Stem Cell Conditioned Media. J Drugs Dermatol. 2023;22(1):82-9.
8. Hoss E, Kollipara R, Alhaddad M, Boen M, Goldman MP. Red Deer Umbilical Cord-Derived Stem Cell Conditioned Media Combined with Ablative Resurfacing of the Face. J Drugs Dermatol. 2020;19:1044-8.
9. Alhaddad M, Boen M, Wu DC, Goldman MP. Red Deer Umbilical Cord Lining Mesenchymal Stem Cell Extract Cream for Rejuvenation of the Face. J Drugs Dermatol. 2019;18(4):363-6.
10. Kim J, Kim B, Kim S, Lee YI, Kim J, Lee JH. The effect of human umbilical cord blood-derived mesenchymal stem cell media containing serum on recovery after laser treatment: A double-blinded, randomized, split-face controlled study. J Cosmet Dermatol. 2020;19(3):651-6.
11. Agha RA, Sohrabi C, Mathew G, Franchi T, Kerwan A, O'Neill N, et al. The PROCESS 2020 Guideline: Updating Consensus Preferred Reporting of CasE Series in Surgery (PROCESS) Guidelines. Int J Surg. 2020:84:231-5.
12. Shoshani D, Markovitz E, Monstrey SJ, Narins DJ. The modified Fitzpatrick Wrinkle Scale: a clinical validated measurement tool for nasolabial wrinkle severity assessment. Dermatol Surg. 2008 Jun:34 Suppl 1:S85-91; discussion S91.
13. Calecim Professional Serum.
14. QuantifiCare 3D Photography systems.
15. Moers-Carpi M, Vogt S, Santos BM, Planas J, Vallve SR, Howell DJ. A multicenter, randomized trial comparing calcium hydroxylapatite to two hyaluronic acids for treatment of nasolabial folds. Dermatol Surg. 2007;33 Suppl 2:S144-51.
16. Paasch U, Bodendorf MO, Grunewald S, Simon JC. Skin rejuvenation by radiofrequency therapy: methods, effects and risks. JDDG: Journal der Deutschen Dermatologischen Gesellschaft. 2009;7:196-203.
17. Jo H, Brito S, Kwak BM, Park S, Lee MG, Bin BH. Applications of

Mesenchymal Stem Cells in Skin Regeneration and Rejuvenation. Int J Mol Sci. 2021;22.

18. Kim YJ, Seo DH, Lee SH, Lee SH, An GH, Ahn HJ, et al. Conditioned media from human umbilical cord blood-derived mesenchymal stem cells stimulate rejuvenation function in human skin. Biochem Biophys Rep. 2018;16:96-102.