Clinical, Cosmetic and Investigational Dermatology Dovepress

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Sustained Repigmentation in Vitiligo and Leukodermas Using Melanocyte–Keratinocyte Transplantation: 7 Years of Data

Nuttaporn Nuntawisuttiwong*, Punyanut Yothachai*, Teerapat Paringkarn, Chayada Chaiyabutr, Chanisada Wongpraparut, Narumol Silpa-archa

Department of Dermatology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand

*These authors contributed equally to this work

Correspondence: Narumol Silpa-archa, Department of Dermatology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand, Tel +66 2419 4333, Email doctornarumol@gmail.com

Background: The autologous non-cultured melanocyte–keratinocyte transplantation procedure (MKTP) has emerged as an effective treatment for various types of vitiligo and leukodermas. However, there is limited data on the long-term outcomes of the MKTP, especially in Thai patients.

Objective: To assess the long-term efficacy and safety of the MKTP in patients with vitiligo and other leukodermas.

Methods: This retrospective observational study analyzed data from 23 patients who underwent the MKTP for vitiligo and other leukodermas at the Siriraj MKTP Clinic, Thailand, and had a follow-up period exceeding 12 months. Clinical characteristics and MKTP specifics were evaluated. Repigmentation outcomes were assessed using the Vitiligo Area Scoring Index (VASI).

Results: Of the 23 patients (24 treated lesions), 78.3% had segmental vitiligo, while the others had nevus depigmentosus, nonsegmental vitiligo, or piebaldism. Most lesions (70.8%) were located on the face. At the 12-month follow-up, repigmentation showed an 80.8% ± 19.3% VASI improvement, which was sustained over 84 months with an 80%–90% VASI improvement. There was no statistically significant difference in repigmentation outcomes between facial and non-facial lesions.

Conclusion: The MKTP demonstrated long-term efficacy and safety in treating vitiligo and other leukodermas, with sustained repigmentation over 84 months. These findings support the use of the MKTP as an effective treatment option for patients with refractory vitiligo and leukodermas, particularly within Thai populations.

Keywords: autologous non-cultured epidermal suspension, melanocyte–keratinocyte transplantation procedure, nevus depigmentosus, piebaldism, repigmentation, vitiligo

Introduction

Vitiligo is characterized by depigmented patches on the skin resulting from melanocyte destruction, with an incidence of 0.5%–1% in the general population.[1] Vitiligo can manifest anywhere on the body, with common sites including the face, chest, hands, armpits, and groin.[2] Other leukodermas, such as nevus depigmentosus and piebaldism can cause similar white patches.[3] Nevus depigmentosus is a rare congenital hypopigmentation distinguished by isolated, well-defined hypopigmented lesions with uneven borders. These lesions are most typically found on the trunk, extremities, and face. Although the specific pathophysiology is unknown, the hypothesized pathogenesis is a transportation defect from melanocyte to keratinocyte.[4] Piebaldism is an autosomal dominant condition that affects melanocyte migration and development, resulting in isolated congenital leukoderma and poliosis in a characteristic ventral midline pattern. Treatment for piebaldism includes skin grafting, cell transplantation, and camouflage techniques.[5] Both vitiligo and other leukodermas significantly impact patients' mental health, quality of life, and social interactions, particularly in individuals with darker skin tones.[1,3]

Received: 3 July 2024
Accepted: 13 October 2024
Published: 2 November 2024

Treatments for vitiligo and other leukodermas primarily involve medication, phototherapy, and surgical interventions. Surgical therapies are increasingly gaining acceptance, especially among patients with refractory vitiligo, where conventional treatments show limited efficacy.[6]

The autologous non-cultured melanocyte–keratinocyte transplantation procedure (MKTP) is a cell-based surgical technique that is effective in treating stable vitiligo. The MKTP was first developed in 1992 by Gautier and Surleve-Bazille,[7] and it remains a frequently utilized grafting method among dermatologists. This procedure involves harvesting a small skin sample, isolating melanocytes, and transplanting them to depigmented areas to restore pigmentation.[8] The advantages of the MKTP include a one-day surgical process, minimal side effects, and the capacity to treat extensive vitiliginous regions.[3]

An increasing number of patients are opting for the MKTP. While short-term outcomes associated with the use of the MKTP for vitiligo and nevus depigmentosus have been documented in Thailand,[9] data on long-term outcomes are limited. Assessing the long-term efficacy of the MKTP in patients with more than a year of follow-up is essential. This information will aid dermatologists in selecting appropriate candidates and optimizing treatment strategies for vitiligo and other leukodermas, particularly in Thai populations.

Methods

Patient Selection

This retrospective cohort study examined the outcomes of the MKTP in patients with leukodermas treated at the Siriraj MKTP Clinic, Siriraj Hospital, Mahidol University, Bangkok, Thailand. The study (Protocol No Si 851/2023) was approved by Siriraj Institutional Review Board, on November 7th 2023. The inclusion criteria included patients who underwent MKTP surgery for vitiligo or other leukodermas (such as piebaldism and nevus depigmentosus) with a minimum follow-up period of 12 months. Vitiligo patients were required to have disease stability for at least 6 months, characterized by the absence of new lesions or progression of existing lesions. No washout period for prior treatments was necessary, but patients with a history of keloid formation were excluded. Patient consent for the review of medical records was waived due to the retrospective design of the study, which posed minimal risk to patients. All patient data were anonymized and managed with strict confidentiality, in full compliance with the Declaration of Helsinki. The demographic and clinical data retrieved from medical records encompassed age, age at disease onset, sex, anatomical treatment areas, number of leukoderma lesions, and type and number of treated lesions. Informed consent for the publication of all clinical images included in this manuscript was obtained from the respective patients.

MKTP Technique

A single dermatologist (N.S.) performed the MKTP on individual patients, following the protocol described by Huggins et al.[8] An ultrathin skin sample, approximately one-fifth to one-tenth the size of the recipient area, was harvested using a dermatome blade from the lateral buttock or anterior thigh. The sample was incubated in an enzyme solution to separate the epidermis (which contained melanocytes) from the dermis (which was discarded). The isolated epidermis was broken down into small pieces and centrifuged to create a cell suspension enriched with melanocytes. The recipient area was dermabraded until pinpoint bleeding occurred. The cell suspension was then applied to the prepared area via a syringe. A dry collagen sheet was placed over the wound, followed by the use of Vaseline gauze and a dry gauze dressing. This dressing was removed after 4–5 days for facial treatments or 1 week for extremities. Postoperative antibiotics were administered for 7 days following the procedure.

Evaluation

Postoperative outcomes were assessed at each follow-up (minimum 12 months) using the Vitiligo Area Scoring Index (VASI). The VASI is a standardized tool that quantifies repigmentation by evaluating the remaining depigmentation and the total treated area.[10] The assessment uses seven percentage levels representing different degrees of repigmentation: 100% (complete depigmentation), 90% (scattered pigment specks), 75% (depigmented area > pigmented area), 50% (equal depigmented and pigmented areas), 25% (pigmented area > depigmented area), 10% (scattered depigmentation),

and 0% (complete repigmentation). The sensitivity of the VASI enables small changes in depigmentation to be detected, thereby increasing the precision of evaluations.

Color matching of the recipient and the donor sites to the surrounding skin was subjectively graded as color-matched, hyperpigmented, hypopigmented, or peripherally hypopigmented. Peripheral hypopigmentation manifests as a rim of hypopigmentation around the repigmented area. Adverse effects, such as scarring and skin atrophy, were also recorded.

Statistical Analysis

Descriptive statistics were used to summarize the data, including frequencies, proportions, means with standard deviations (for normally distributed continuous variables), or medians with interquartile ranges for skewed data. The percentage change in the Vitiligo Area Scoring Index (VASI) improvement over time was calculated using a linear mixed model. A *P* value less than 0.05 was considered to indicate statistical significance. Data analyses were conducted using IBM SPSS Statistics, version 25 (IBM Corp, Armonk, NY, USA).

Results

Demographic and Clinical Data

The study included 23 patients with various types of leukodermas who underwent MKTP surgery for 24 lesions. Segmental vitiligo was the most prevalent diagnosis, affecting 78.3% of the patients. The face and neck were the most common treatment sites, accounting for 70.8% of the patients. Table 1 provides comprehensive details on patient demographics and clinical characteristics. The average patient age was 30.4 years, with disease onset occurring at a median age of 17 years. Most patients had Fitzpatrick skin phototype IV. Before the MKTP, 65.2% of patients had been treated with topical corticosteroids, 69.6% with topical calcineurin inhibitors, and 60.9% with phototherapy.

Table 1 Demographic and clinical characteristics of patients undergoing the melanocyte-keratinocyte transplantation procedure

Characteristics	N (%)
Number of patients	23
Number of treated lesions	24
Sex, N (%) • Female • Male	 16 (69.6) 7 (30.4)
Age, y, mean ± SD	30.4 ± 15.1
Age at onset, y, median (IQR)	17 (9, 35)
Fitzpatrick skin phototype • III • IV	 3 (13.0) 20 (87.0)
Type of lesion (N=23) • Segmental vitiligo • Nonsegmental vitiligo • Piebaldism • Nevus depigmentosus	 18 (78.3) 1 (4.3) 1 (4.3) 3 (13.0)
Location of anatomical lesions (N=24) • Face and neck • Lower extremities	 17 (70.8) 7 (29.2)

(*Continued*)

Table 1 (Continued).

Characteristics	N (%)
Stable time before MKTP, mo	12 (6, 36)
Poliosis	6 (26.1)
Treatment before MKTP (N=23)	
• Topical corticosteroids	15 (65.2)
• Topical calcineurin inhibitors	16 (69.6)
• Systemic corticosteroids	6 (26.1)
• Phototherapy	14 (60.9)
○ Whole body NB-UVB	1 (4.3)
○ Local NB-UVB	3 (13.0)
○ Targeted NB-UVB	1 (4.3)
○ Local PUVA	1 (4.3)
○ Excimer lamp	9 (39.1)
• Others	5 (21.7)

Abbreviations: MKTP, melanocyte-keratinocyte transplantation procedure; NB-UVB, narrowband ultraviolet B; PUVA, psoralen plus ultraviolet A.

Results for the Donor and Grafted Sites

Long-term follow-up ranging from 12 to 84 months indicated favorable outcomes following the MKTP. The mean size of the donor area used for transplantation was 19.3 cm^2, and the median size of the recipient sites treated was 35.3 cm^2. (Table 2) The primary outcome measure—changes in depigmentation via the VASI—demonstrated substantial improvement from baseline at each follow-up interval across all leukodermas. The mean VASI score reduction was 80.8% at 12 months, with sustained repigmentation indicated by an 80%–90% mean reduction over the 84-month follow-up period (Figure 1).

In vitiligo patients, significant improvement in VASI was observed over time, as detailed in Table 3. At the 1-year follow-up, 20 treated lesions demonstrated an average improvement of 80.5% ± 20.9% compared to baseline, with continuously sustained repigmentation over an 84-month period. For nevus depigmentosus, 3 patients showed an average

Table 2 Donor and recipient site characteristics of all treated sites

Characteristics (N=24)	N (%)
Size of donor area, cm^2, mean ± SD	19.3 ± 8.6
Size of recipient area, cm^2, median (IQR)	35.3 (22.8, 66.8)
The ratio between donor-to-recipient site, median (IQR)	0.43 (0.32-0.78)
Donor site	
Color match	
• Good color match	12 (50.0)
• Hyperpigmentation	7 (29.2)
• Hypopigmentation	1 (4.2)
• Hypertrophic scar	4 (16.7)
Recipient site	
Color match	
• Good color match	10 (41.7)
• Hyperpigmentation	8 (33.3)
• Hypopigmentation	6 (25.0)

(*Continued*)

Table 2 (Continued).

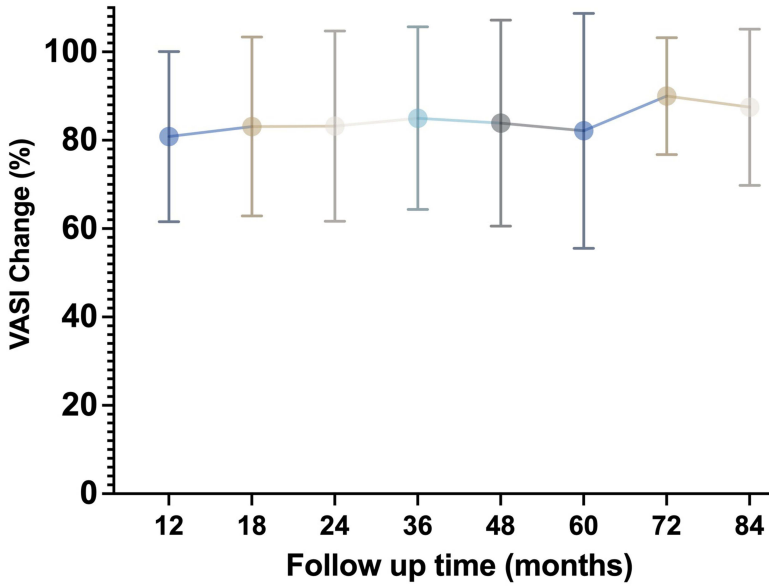
Characteristics (N=24)	N (%)
Peripheral hypopigmentation	2 (8.3)
Treatment after MKTP	
• Topical corticosteroids	3 (12.5)
• Topical calcineurin inhibitors	15 (62.5)
• Systemic corticosteroids	6 (25.0)
• Phototherapy	8 (33.3)
○ Excimer lamp	6 (25.0)
○ Sunlight	2 (8.3)

Abbreviations: MKTP, melanocyte-keratinocyte transplantation procedure.

improvement of 80.0% ± 8.7% at the 1-year follow-up, maintaining 80–90% repigmentation over 36 months. One case of piebaldism exhibited a 90% improvement in VASI at the 1-year follow-up.

Repigmentation, assessed by VASI score improvement, was greater in non-facial areas (82%–100%) than in facial areas (75%–85%). However, the difference between these areas was not statistically significant (Figure 2). Four lesions achieved complete repigmentation, as evidenced by a 100% VASI change (Figures 3–5).

Color matching assessments revealed varying degrees of color matching at the donor and recipient sites (Table 2). Over half (50%) of the donor sites achieved good color matching, 29.2% exhibited hyperpigmentation, and 4.2% showed hypopigmentation. For the recipient sites, 41.7% had good color matching, while hyperpigmentation and hypopigmentation were noted in 33.3% and 25.0% of the patients, respectively.



		12	18	24	36	48	60	72	84
All cases	Mean	80.83	83.13	83.21	85.00	83.89	82.14	90.00	87.50
	SD	19.26	20.24	21.54	20.67	23.29	26.59	13.23	17.68
	N	24	16	14	12	9	7	3	2

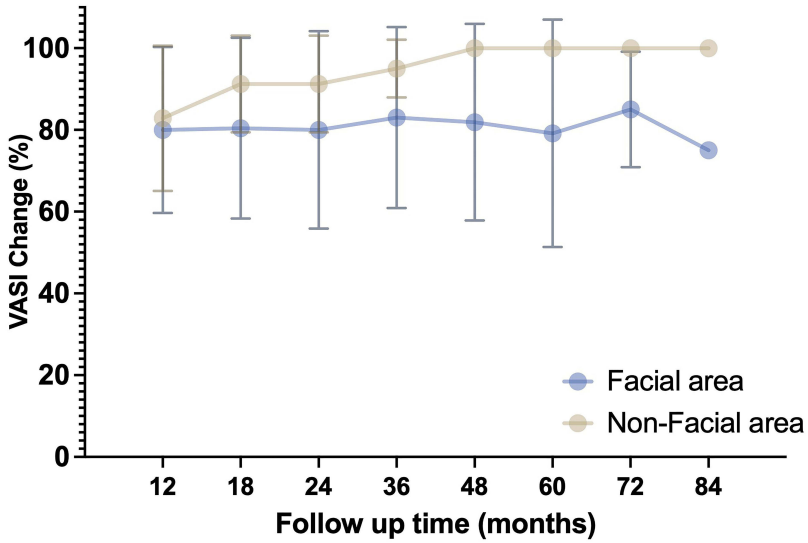
Figure 1 Percent improvement in Vitiligo Area Scoring Index at treated sites over 84 months of follow-up (N=24).
Abbreviations: VASI, Vitiligo Area Scoring Index.

Table 3 Percent Improvement in Vitiligo Area Scoring Index in Vitiligo Patients (N=20) Over 84 Months of Follow-Up

Follow-up time	N	Improvement in VASI (%, Mean ± SD)
1 year	20	80.50 ± 20.89
1.5 years	14	83.21 ± 21.54
2 years	12	83.33 ± 23.19
3 years	11	84.55 ± 21.62
4 years	9	83.89 ± 23.29
5 years	7	82.14 ± 26.59
6 years	3	90.00 ± 13.23
7 years	2	87.50 ± 17.68

Abbreviation: VASI, Vitiligo Area Scoring Index.

Following the MKTP, 62.5% of patients were treated with topical calcineurin inhibitors, and 25.0% received subsequent phototherapy with an excimer lamp. However, neither of these adjunct treatments significantly impacted repigmentation outcomes.



		12	18	24	36	48	60	72	84
Facial area	Mean	80.0	80.4	80.0	83.0	81.9	79.2	85.0	75.0
	SD	20.3	22.1	24.2	22.1	24.0	27.8	14.1	0.0
	N	17	12	10	10	8	6	2	1
Non-Facial area	Mean	82.9	91.3	91.3	95.0	100.0	100.0	100.0	100.0
	SD	17.8	11.8	11.8	7.1	0.0	0.0	0.0	0.0
	N	7	4	4	2	1	1	1	1
P-value		*0.737*	*0.241*	*0.268*	*0.211*	†	†	†	†

*P-value (Time, Group, Time*Group)* = 0.1940, 0.7504, 0.4985 respectively
† Comparison cannot be performed *due to the number of non-facial areas (N=1)*

Figure 2 Percent improvement in Vitiligo Area Scoring Index by anatomical location over 84 months of follow-up (N=24). Statistical significance at *P-value*<0.05.
Abbreviations: VASI, Vitiligo Area Scoring Index.

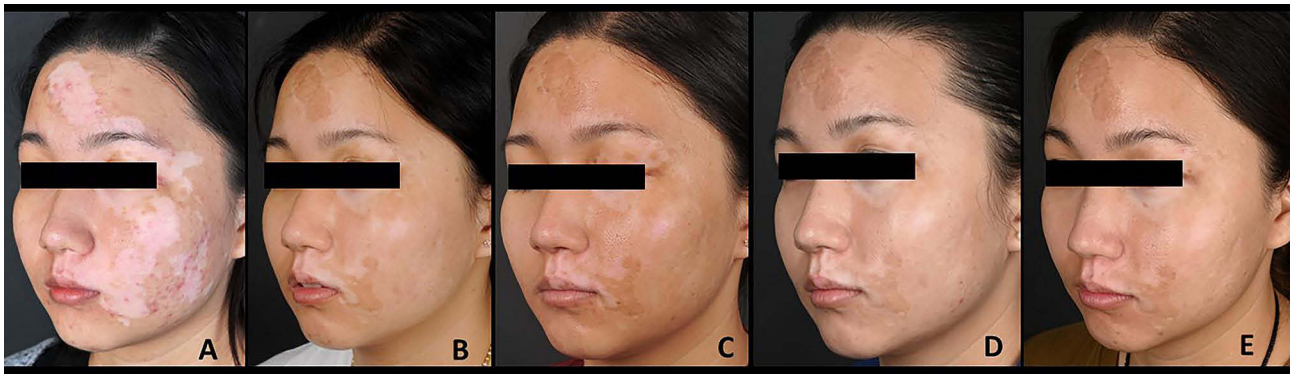


Figure 3 Segmental vitiligo on facial area (**A**) Baseline (**B**) 18 months after the MKTP (**C**) 24 months after the MKTP (**D**) 36 months after the MKTP (**E**) 60 months after MKTP.
Abbreviations: MKTP, melanocyte-keratinocyte transplantation procedure.

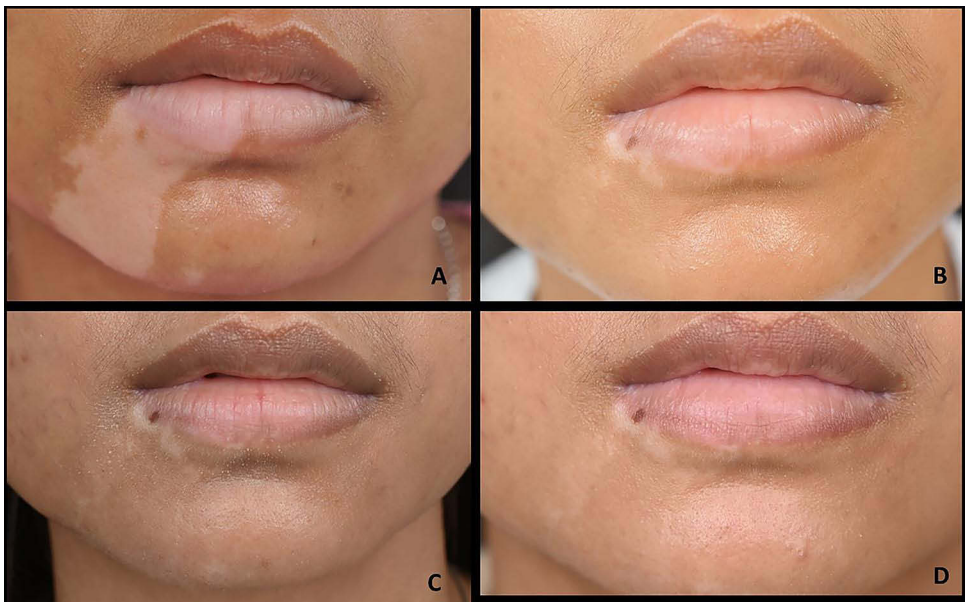


Figure 4 Segmental vitiligo on facial area (**A**) Baseline (**B**) 12 months after the MKTP (**C**) 24 months after the MKTP (**D**) 36 months after the MKTP.
Abbreviations: MKTP, melanocyte-keratinocyte transplantation procedure.

Adverse Effects

Adverse effects were documented in a minority of patients. Hypertrophic scarring, noted in 16.7% of donor sites, was the most prevalent adverse effect. Peripheral hypopigmentation was observed in 8.3% of the recipient sites, with no scarring noted in the recipient areas. Two patients in our retrospective cohort exhibited disease progression of vitiligo after the MKTP. Both patients had segmental vitiligo on the face and had maintained disease stability for 6 and 12 months before the MKTP; one of these patients also presented with poliosis before the procedure.

Discussion

This study evaluated the long-term outcomes of the MKTP in treating vitiligo and other leukodermas in Thailand. We analyzed data from all patients at our clinic who underwent the MKTP and had follow-up periods exceeding 1 year. Our findings indicated considerable improvements in repigmentation, as measured by the VASI score, with patients achieving a mean improvement of 80.8% at the 12-month follow-up. This repigmentation rate remained consistent, ranging between 80% and 90%, over a long-term follow-up of up to 84 months for all leukodermas studied. However, due to

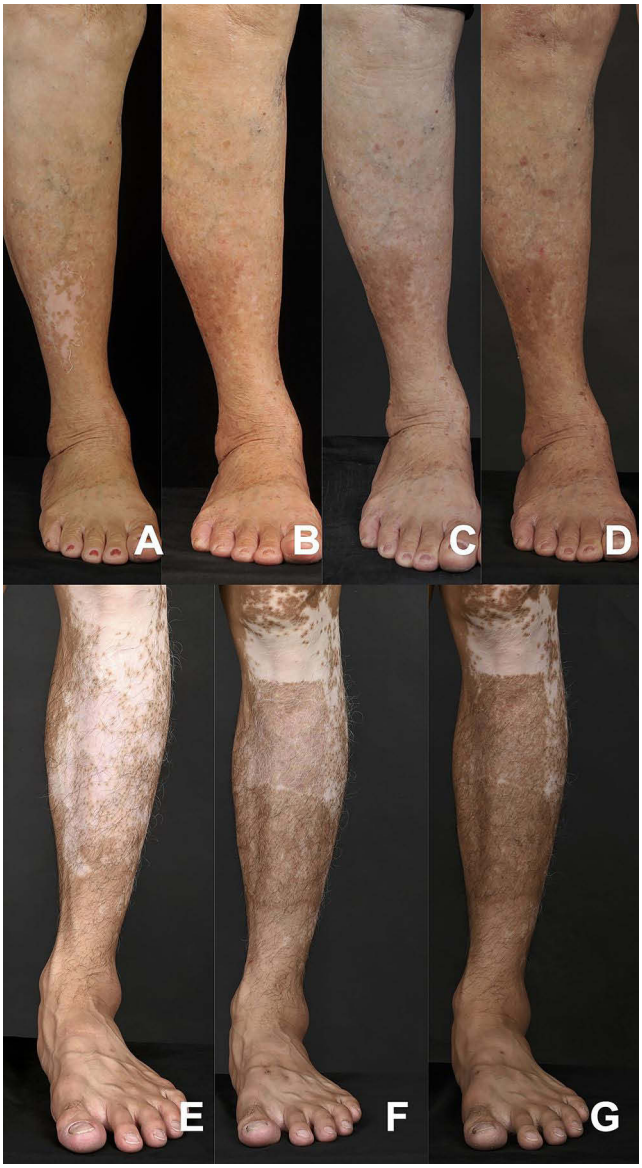


Figure 5 Vitiligo on non-facial area (Non-segmental vitiligo: (**A-D**)) (Segmental vitiligo: (**E-G**)) (**A**) Baseline (**B**) 12 months after the MKTP (**C**) 24 months after the MKTP (**D**) 36 months after the MKTP (**E**) Baseline (**F**) 12 months after the MKTP (**G**) 18 months after the MKTP.
Abbreviations: MKTP, melanocyte-keratinocyte transplantation procedure.

the limited number of nonsegmental vitiligo and other leukoderma patients, we could not compare outcomes between different leukoderma groups. Notably, segmental vitiligo constituted the majority of our cohort (78.3%).

The overall repigmentation rates observed in our study are consistent with prior research. Gan et al[11] reported that 83% of patients achieved at least 75% repigmentation, which was sustained for more than 60 months. Similarly, Zhang et al[12] conducted follow-ups for up to 108 months and reported excellent repigmentation in more than half of the lesions, with pigment retention persisting throughout the follow-up period. Silpa-Archa et al[13] also reported that more than 50% of patients maintained an improvement in VASI scores of more than 75% for 72 months after the MKTP, with segmental vitiligo showing superior outcomes compared to nonsegmental vitiligo. The findings of Silpa-archa et al align with the predominance of segmental vitiligo in our cohort.

The MKTP has also shown efficacy in treating other leukodermas. Van Geel et al[14] reported successful outcomes in one patient with nevus depigmentosus and three patients with piebaldism, with average repigmentation rates of 78% and 90%, respectively. Mulekar et al[15] noted that the repigmentation rate ranged from 80% to 100% in three patients with

nevus depigmentosus, although two presented with uneven repigmentation quality. In contrast, Maghfour et al[16] observed only a 51.8% improvement in the VASI for other leukodermas and piebaldism. In our cohort, patients with nevus depigmentosus and piebaldism treated with the MKTP showed 75%–90% improvement over a two-year follow-up period.

Although non-facial lesions exhibited slightly better repigmentation than facial lesions, there was no statistically significant difference between these groups in our cohort, which is consistent with the findings of Zhang et al.[12] However, the outcome varied based on the location of the lesion.[17] Compared to other vitiligo treatments, such as narrowband ultraviolet B (NB-UVB) therapy, which has the highest repigmentation rate in facial areas,[18] our findings support the efficacy of the MKTP across multiple anatomical sites, including the face, neck, trunk, and extremities.

With the MKTP, recipient site preparation is critical for successful transplantation. Preparation involves separating the epidermis from the underlying dermis and directly applying epidermal cell suspensions to facilitate repigmentation and engraftment of transplanted basal layer cells.[19] Various techniques for recipient site preparation have been described. Gupta et al[20] reported no significant difference in repigmentation or side effects between erbium-doped yttrium aluminum garnet (Er:YAG) laser ablation and mechanical methods. Silpa-Archa et al[21] observed superior repigmentation outcomes with dermabrasion compared to fractional carbon dioxide laser therapy, reporting VASI improvement rates of 84% and 73.5%, respectively. Our long-term outcomes highlight that dermabrasion preparation achieved over 80% sustained repigmentation. This effect lasted up to 84 months without major side effects. Dermabrasion, therefore, proves to be an effective and minimal-scarring method that offers accessibility and affordability.

Post-transplantation care is crucial, especially during the initial 48–72 hours when transplanted cells integrate into the recipient tissue. Our transplantation procedures employ collagen dressings, which are widely recognized for promoting cell survival and migration.[19] Gan et al[11] found that collagen dressings significantly enhanced repigmentation outcomes compared with hyaluronic acid suspensions at 12 months. Similarly, Singh et al[22] reported that, compared with conventional dressings, collagen dressings facilitated sterile conditions and earlier formation of healthy granulation tissue. Our findings further emphasize the favorable long-term outcomes of using collagen dressings in the MKTP.

Peripheral hypopigmentation was observed in 8.3% of our cohort. Previous studies by Wu et al[23] and van den Boorn et al[24] attributed this to cytotoxic CD8+ cells in perilesional skin. These cells induce extensive autologous melanocyte apoptosis due to melanocyte antigen recognition, leading to melanocyte-specific killing and subsequent disappearance post-transplantation. To mitigate this side effect, Mutalik et al[25] tested a postoperative cyclosporine regimen: 3 mg/kg for 3 weeks, followed by 1.5 mg/kg for the next 6 weeks. This regimen improved repigmentation by inhibiting perilesional CD8+ T cells. Additionally, Zhang et al[12] recommended pre-transplantation NB-UVB to induce apoptosis in skin-infiltrating T cells, resulting in better outcomes than without pre-transplantation NB-UVB. Regarding other adverse effects, we found four hypertrophic scars at the donor sites, but no infections or serious side effects were reported. This is consistent with the findings of Silpa-archa et al[13] who reported two cases of hypertrophic scars and 18% peripheral hypopigmentation. The lack of serious side events in our cohort supports the notion that MKTP is a relatively safe technique for repigmentation in patients with refractory stable vitiligo and other leukodermas.

A minimum of 6 months of disease stability is required to meet the inclusion criteria for surgical procedures.[26] However, two patients in our cohort exhibited disease progression: one with 6 months and the other with 12 months of stability. Rao et al[27] observed a higher lesional CD8+ T-cell count in vitiligo patients with shorter disease-stability durations (3–12 months) than in those with longer durations. Refat et al[28] also demonstrated a negative correlation between the CD8+ T-cell count at the recipient site and repigmentation following the MKTP. This finding indicates that some patients who were clinically stable for 12 months still harbored significant CD8+ T-cell populations, suggesting ongoing disease activity. The occurrence of disease progression in our cohort underscores the importance of thorough clinical assessment and patient-reported disease stability as crucial criteria before proceeding with transplantation. Ensuring disease stability is the most critical factor for a successful outcome.[17]

In our cohort, 25% of patients received phototherapy post-transplantation, but this did not significantly impact repigmentation outcomes. This finding is consistent with that of Gan et al,[11] who reported that targeted phototherapy with MultiClear (Curelight) after grafting did not enhance repigmentation. Similarly, Tawfik et al[29] found no statistically significant differences between groups with and without NB-UVB treatment. However, Wang et al[30] demonstrated that

combining phototherapy with melanocyte transplantation resulted in higher expression of tyrosinase and Melan-A, leading to better repigmentation outcomes and a lower incidence of the Köebner phenomenon. Due to the retrospective nature of our study, the phototherapy regimens varied among patients. Further studies, particularly on the clinicopathological correlation of phototherapy and other immunomodulators with transplantation, should be considered.

This study has several limitations, including its small sample size and retrospective design. Many patients were lost to follow-up, lowering the sample size and limiting our statistical power to identify all possible changes in association across groups. Furthermore, the data were gathered from current medical records rather than through prospective surveillance, which could result in incomplete or missing information. A prospective case-control study could collect more reliable data, eliminate bias, and better establish causal linkages. Future research should consider this approach to strengthen the findings.

Conclusions

Our study demonstrated the long-term efficacy of the MKTP in treating vitiligo and other leukodermas in both the facial and non-facial areas, achieving sustained repigmentation exceeding 80% over an 84-month follow-up period. The use of dermabrasion for recipient site preparation and post-transplantation collagen dressing contributed significantly to these positive outcomes. Although some patients may exhibit peripheral hypopigmentation and disease progression, careful patient selection remains crucial. Limitations include the small sample size and retrospective study design, which restricted statistical power and data completeness. Further research is warranted to address study limitations and validate our findings regarding adjuvant therapy.

Acknowledgments

The authors would like to thank Ms.Julaporn Pooliam for her assistance in statistical analysis.

Disclosure

The authors report no conflicts of interest in this work.

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