

Research Article

Effect of robot-assisted gait training on the biomechanical properties of burn scars: a single-blind, randomized controlled trial

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Abstract

Background: Robot-assisted gait training (RAGT) is more effective in the range of motion (ROM) and isometric strength in patients with burns than conventional training. However, concerns have been raised about whether RAGT might negatively affect the scars of patients with burns. Therefore, we investigated the effects of RAGT-induced mechanical load on the biomechanical properties of burn scars.

Methods: This was a single-blind, randomized clinical trial conducted on inpatients admitted to the Department of Rehabilitation Medicine between September 2020 and August 2021. RAGT was conducted for 30 min per day, five days a week for 12 weeks and the control group received conventional gait training for 12 weeks. The pre-training ROM of lower extremity joints was evaluated and the levels of melanin, erythema, trans-epidermal water loss, scar distensibility and elasticity were assessed before training and at 4 and 12 weeks after training. Finally, 19 patients in the gait assistance robot (GAR) group and 20 patients in the control group completed the 12-week trial and all evaluations.

Results: There were no significant differences in the epidemiologic characteristics, pre-training ROM of joints and pre-training biomechanical properties of the burn scar between the groups ($p > 0.05$ for all). None of the patients experienced skin abrasion around the burn scar where the fastening belts were applied or musculoskeletal or cardiovascular adverse events during the training. Scar thickness significantly increased in both groups ($p = 0.037$ and $p = 0.019$) and scar distensibility significantly decreased in the control group ($p = 0.011$) during the training. Hysteresis was significantly decreased in the GAR group during the training ($p = 0.038$). The GAR and control groups showed significant difference in the change in the values of hysteresis between pre-training and 12 weeks after training ($p = 0.441$ and $p = 0.049$).

Conclusions: RAGT significantly decreased hysteresis in hypertrophic burn scars and did not cause a significant decrease in skin distensibility. Moreover, no skin complications around the burn scars were detected during RAGT.

Trial registration

This study registered on the Clinical Research Information Service (KCT0005204).

Key words: Robot-assisted gait training, Burn, Scar biomechanical properties, Hysteresis, Burn rehabilitation

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Highlights

- This study clarified the effect of robot-assisted gait training on biomechanical properties of burn scars.
- Robot-assisted gait training had no negative effects on burn scars.
- Robot-assisted gait training decreased hysteresis on burn scars.

Background

The primary goals of burn rehabilitation medicine are preventing the formation of burn scar contracture, improving the limited range of motion (ROM) of joints and limiting functional restrictions [1]. In particular, scar contracture of the lower extremities can lead to pain during walking and limited ROM of the hip, knee and ankle joints, which can result in gait disturbance [2,3]. Appropriate and sufficient rehabilitation therapy following burn injury can decrease hypertrophic scar formation and delay the progression of scar contracture in burn survivors [1,4]. Conventional rehabilitation therapy for patients with burns with scar contracture of the lower extremities includes passive joint ROM training with disconnected movements, gait training using walking aids and manual therapy by a physical therapist [5]. The latest trends in rehabilitation therapy emphasize the motor learning theory, which states that motor skills can be learned through intensive, repetitive training mimicking the patient's motion [6]. Task-specific training based on the motor learning theory is reportedly more effective than conventional rehabilitation therapy [7]. Accordingly, intensive, repetitive training of normal gait motion has been applied by experienced physical therapists and, more recently, by gait assistance robots (GARs) for patients with gait disturbance. GARs are pre-programmed to induce lower extremity movements following normal physiological gait patterns and assist gait training by therapists. Therefore, it can improve the repeatability of gait kinematics and can thereby reduce the time and physical labour requirements of therapists [3,8–11].

In our previous studies, we showed that robot-assisted gait training (RAGT) in patients with burns increased isometric strength and ROM of the lower extremities more significantly than does conventional training [3,11]. However, concerns exist regarding the potential negative effects of RAGT on the scars of patients with burns despite the absence of skin complications during our study. To our knowledge, no studies have demonstrated or published the effects of RAGT-induced mechanical load on the biomechanical properties of burn scars despite the expansion of robotic technologies in the field of burn rehabilitation medicine. Furthermore, applying mechanical loads to re-epithelializing wounds of mouse skin stimulated the formation of hypertrophic scars by reducing cellular apoptosis [12], and mechanical stretching enhanced hypertrophy and hyperplasia in the pulmonary artery [13]. Skin safety studies for RAGT are needed to revitalize the use of GAR in rehabilitation therapy for patients with burns. Therefore, GAR was applied to the rehabilitation therapy of patients with burns with limited ROM in the lower

extremities to investigate the effects of RAGT on the scar biomechanical properties.

Methods

Study population and ethics statement

This was a single-blind, randomized clinical trial conducted between September 2020 and August 2021. A total of 46 patients admitted to the burn centre in the Department of Rehabilitation Medicine were recruited. The inclusion criteria were (1) adult (19 years or older) patients with burn scar contracture in the lower extremities, (2) sufficient cognitive function to control the robot, (3) no neuromuscular diseases, which could be associated with weakness in the lower extremities, and (4) written informed consent provided for trial inclusion. Six of them were excluded for the following reasons: (1) duration of <2 months from burn injury to the evaluation because of a high risk of skin abrasion during RAGT in our previous pilot study ($n=3$); (2) weight of ≥ 100 kg or height of <150 cm or ≥ 185 cm due to exceeding the constraints of the robot ($n=1$); (3) bleeding tendency in the scar area ($n=1$); and (4) history of fibula fracture ($n=1$) [3,11].

Randomization and blinding

The remaining 40 burn patients were enrolled and numbers were assigned according to the order of admission of 40 patients with scar contracture in the lower extremities. Then a computer program was used to randomly divide them into the GAR group for RAGT ($n=20$) and the control group for conventional gait training ($n=20$) (Figure 1). An experienced physical therapist, who was not involved in the rehabilitation training, measured the ROMs of the joints in the lower extremities. A research assistant, who was not involved in the rehabilitation training, performed a skin test for the scar biomechanical properties. The present study and study protocol were approved by the Institutional Review Board (HG2020-006) and registered on the Clinical Research Information Service (KCT0005204). All patients voluntarily participated in the study after providing written informed consent.

RAGT

The ROM of the joints in the lower extremities was evaluated to test pre-training homogeneity before training. Flexion and extension ROM in the hip, knee and ankle joints were evaluated using a portable goniometer following a standardized

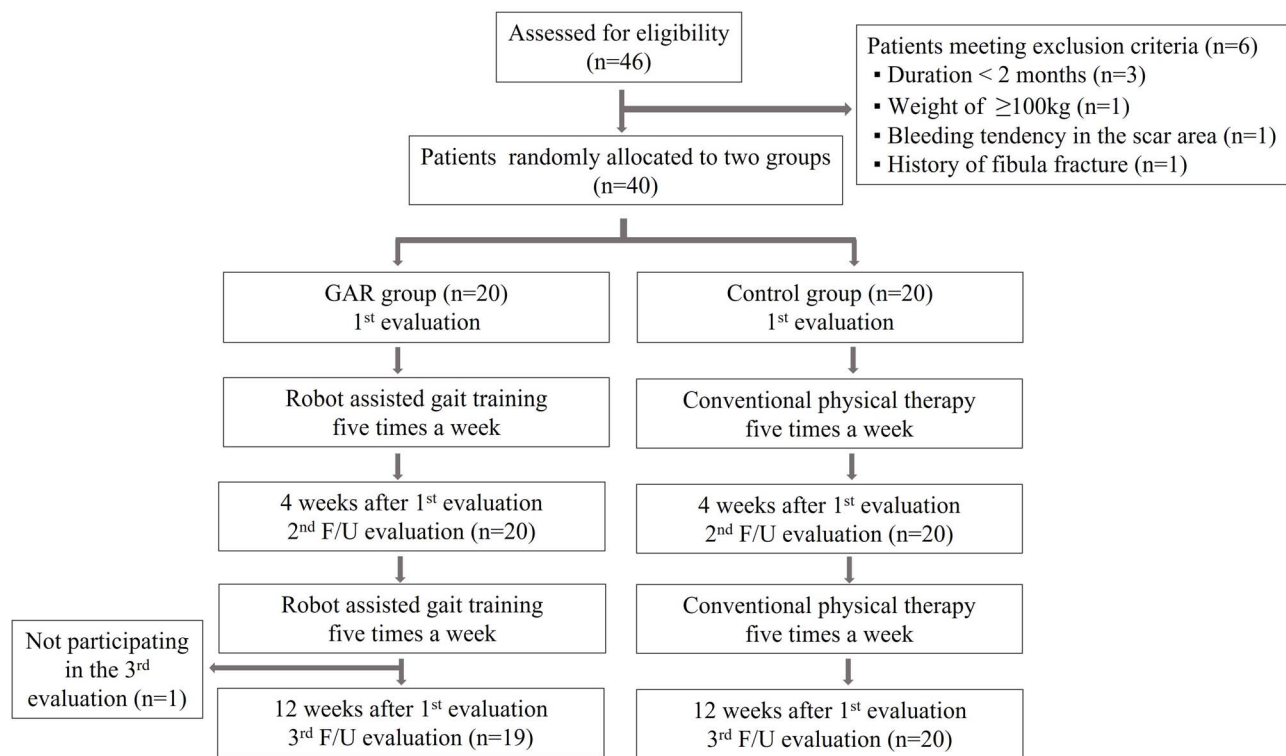


Figure 1. Flow chart of patient enrollment and participation

technique by an experienced physical therapist, who was not involved in the rehabilitation training [14]. The GAR group received gait training using the SUBAR® (CRETEM Co. Ltd, Anyang-si, South Korea) (Figure 2). The SUBAR® consists of an exoskeleton that supports the legs and an operating device that assists gait. The robot provides force to the patient for walking. The leg exoskeleton was adjusted for each patient based on hip-to-knee and knee-to-foot length measurements that were taken prior to RAGT. Both lower limbs were placed into the exoskeleton and the thighs and legs were firmly fixed with the fastening belts. The gait speed and knee ROM were gradually adjusted according to improvements in joint motion and gait function. The setup could be operated directly by the patient or be controlled remotely by the physical therapist for the safety of the patient. The RAGT consisted of stepping in place, forward gait and backward gait. The training was conducted for 30 min per day, 5 days a week for 12 weeks. The control group received conventional gait training, including ROM and strengthening exercise training in the sitting or standing position, weight-bearing training on the side with leg weakness and balance training to facilitate normal gait pattern.

Assessment of the scar biomechanical properties

A skin test was conducted by a research assistant in an independent and blinded fashion before training and at 4 and 12 weeks after training (Figure 3). To ensure consistency of the scar location, a translucent linear low-density



Figure 2. Burn patient undergoing robot-assisted gait training using the SUBAR®



Figure 3. A skin test was conducted on the burn scars of eligible patients before training and at 4 and 12 weeks after training. (a) Patient with the initial burn injury, (b) Mexameter® for measuring the levels of melanin and erythema, (c) Tewameter® for measuring trans-epidermal water loss and (d) Cutometer® for measuring scar distensibility and elasticity

polyethylene film, Cleanwrap® (CLEANWRAP Co., Ltd, Gimhae-si, South Korea), was applied to the measurement site. For identification of the region to be measured, remarkable landmarks and a circle with a 3-cm diameter were drawn on the film as in previous studies [15,16]. The levels of melanin and erythema were evaluated using a Mexameter MX18® (Courage-Khazaka Electronics GmbH, Cologne, Germany), with a higher value representing a darker and redder scar. Trans-epidermal water loss, which represents skin barrier function, was investigated using a Tewameter® (Courage-Khazaka Electronics GmbH, Cologne, Germany). Relative humidity was maintained at 40–50% and room temperature at 20–25°C during skin assessment [17]. Scar distensibility and elasticity were assessed using a Cutometer SEM 5801® (Courage-Khazaka Electronic GmbH, Cologne, Germany). The skin was pulled upwards by negative pressure for 5 s, followed by 3 s of relaxation. A skin deformation curve was obtained from three measurement cycles (Figure 4). Relative R-parameters, such as R1, $U_f - U_a$; R2, U_a / U_f ; R5, U_r / U_e ; R6, U_v / U_e ; R7, U_r / U_f ; and R9, $R_3 - R_0$, could be derived from U_a , U_e , $U_f = R_0$, U_r and U_v , which are absolute parameters [18]. Absolute parameters are less reliable in hypertrophic scars since these are dependent on the skin thickness. Relative parameters can be used to compare different anatomical sites because these are independent of the skin thickness [19]. Therefore, four parameters, R0, R2, R6 and R9, were selected to compare the biomechanical properties of the burn scars [19–21]. Final distensibility ($R_0 = U_f$) is the length of skin displaced from the initial location by negative pressure. Gross elasticity ($R_2 = U_a / U_f$) is the capacity that the skin exhibits to return to its initial location. Viscoelasticity ($R_6 = U_v / U_e$) is the potency against an interstitial fluid shift, which is higher in firmer skin. Hysteresis ($R_9 = H$) is the difference in the skin distension between the first and last suction, which indicates tiring effects [21]. Scar thickness was measured using an

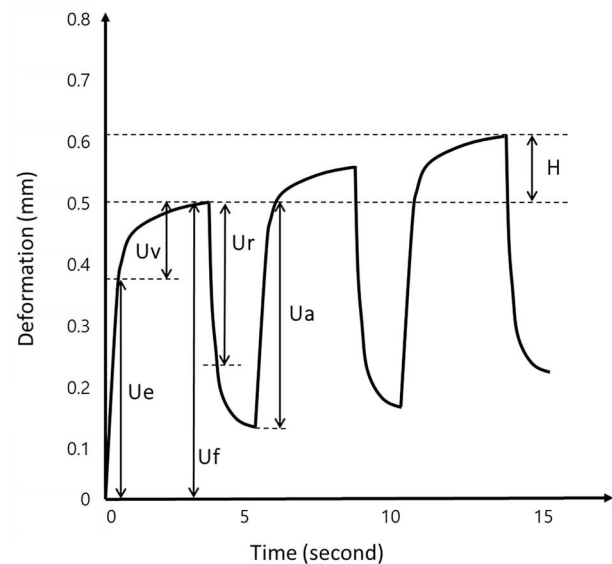


Figure 4. Skin deformation assessments. Four parameters, namely, final distensibility ($R_0 = U_f$), gross elasticity ($R_2 = U_a / U_f$), viscoelasticity ($R_6 = U_v / U_e$) and hysteresis ($R_9 = H$), were used to investigate the effect of robot-assisted gait training on burn scars

E-CUBE 7® ultrasound machine (Alpinion Medical Systems Co., Ltd, Anyang-si, Korea).

Primary outcome measures

The primary outcome measures to compare the biomechanical properties of the burn scars were R0, R2, R6 and R9 parameters, and scar thickness before RAG training and at 4 and 12 weeks after training.

Secondary outcome measures

Secondary outcome measure was the presence or absence of skin complication around the burn scars during RAGT.

Statistical analyses

All statistical analyses were performed using SPSS version 21 (IBM Corp., Armonk, NY, USA), with $p < 0.05$ considered statistically significant. To estimate the sample size with sufficient statistical power, GPower (version 3.1.9.7, Franz Faul, Universität Kiel, Germany), which is a freely-available statistical software package, was used (effective size f of 0.25; alpha level of 0.05; statistical power of 80%) [22]. A total of 40 patients were included with a dropout rate of 10%. The intention-to-treat analysis was conducted at the same time to avoid the bias caused by the elimination of randomization. Numerical data are presented as mean $\pm$ standard deviation or median (interquartile range) and categorical data as a number (%). The Shapiro–Wilk test was used for the assumption of normality. To evaluate the pre-training homogeneity between the GAR and control groups, the independent t- and Mann–Whitney U tests for numeric data and Fisher’s exact test for categorical data were used. The effect of RAGT-induced mechanical load on the biomechanical properties of burn scars throughout the training regimen was analyzed

Table 1. Patient demographics

	GAR group	Control group	P value
Male : female, <i>n</i> (%)	17(85) : 3(15)	16(80) : 4(20)	1.000 ^a
Age (years)	54.1 ± 9.5	55.1 ± 12.3	0.550 ^b
Height (cm)	170.7 ± 5.5	172.9 ± 5.0	0.196 ^c
Weight (kg)	68.1 ± 9.9	69.4 ± 7.2	0.645 ^c
Percent of TBSA (%)	29.1 ± 15.2	25.0 ± 17.0	0.343 ^b
Duration since burn injury (days)	76 (63.5, 109.0)	70 (63.3, 114.0)	0.634 ^b
Types of burn, <i>n</i> (%)			1.000 ^a
Flame burn	12 (60)	11 (55.0)	
Scalding burn	5 (25)	4 (20.0)	
Contact burn	1 (5)	2 (10.0)	
Electrical burn	2 (10)	3 (15.0)	
Scar site for evaluation, <i>n</i> (%)			0.841 ^a
Thigh	4 (20)	3 (15.0)	
Knee	8 (40)	10 (50.0)	
Leg	8 (40)	7 (35.0)	

Data are presented as mean ± standard deviation or median (25% percentile, 75% percentile) for continuous variables or as numbers (%) for categorical variables. GAR gait assistance robot, TBSA total body surface area

^aFisher's exact test

^bMann-Whitney *U* test

^cIndependent *t*-test

Table 2. Pre-training scar biomechanical properties and pre-training joint range of motion

	GAR group (<i>n</i> = 20)	Control group (<i>n</i> = 20)	P value
Biomechanical property			
Melanin (AU)	164.7 ± 42.6	198.8 ± 77.0	0.093 ^a
Erythema (AU)	472.6 ± 82.9	455.5 ± 88.0	0.530 ^a
TEWL (g/h/m ²)	13.9 (12.1, 17.2)	15.7 (10.1, 17.8)	0.794 ^b
Final distensibility (R0 = Uf)	0.58 (0.37, 1.54)	0.78 (0.33, 1.20)	0.963 ^b
Gross elasticity (R2 = Ua/Uf)	0.64 (0.08, 0.74)	0.61 (0.02, 0.73)	0.449 ^b
Viscoelasticity (R6 = Uv/Ue)	0.30 (0.02, 0.43)	0.34 (0.01, 0.47)	0.931 ^b
Hysteresis (R9 = H)	0.063 (0.034, 0.130)	0.065 (0.025, 0.125)	0.815 ^b
Thickness (mm)	1.89 ± 0.46	1.91 ± 0.51	0.922 ^a
ROM of joint (degree)			
Hip flexion	100 (98.5, 100.0)	100 (100.0, 100.0)	0.231 ^b
Hip extension	14.8 ± 9.8	19.2 ± 8.5	0.141 ^a
Knee flexion	109.9 ± 17.7	116.6 ± 13.2	0.179 ^a
Knee extension	−0.5 (−8.0, 0.0)	0 (−0.5, 0.0)	0.606 ^b
Ankle dorsiflexion	19 (14.0, 20.0)	20 (15.0, 20.0)	0.470 ^b
Ankle plantarflexion	40 (20.0, 40.0)	36.5 (20.3, 40.0)	0.696 ^b

Data are presented as mean ± standard deviation or median (25% percentile, 75% percentile). GAR gait assistance robot, AU arbitrary unit, TEWL trans-epidermal water loss, ROM range of motion

^aIndependent *t*-test

^bMann-Whitney *U* test

using one-way repeated-measures analysis of variance and the Friedman test. The independent *t*- and Mann-Whitney *U* tests were used for intergroup comparisons of the change in the values of the scar biomechanical properties between pre-training and 4 and 12 weeks after training.

Results

A total of 40 patients with burns who satisfied the inclusion criteria were enrolled in the study, 39 of whom completed all assessments. All of the 40 patients were included in the

statistical analysis following the intention-to-treat analytic strategy. There were no significant differences in the mean age, height, weight, burned area percent of total body surface area, duration since burn injury or type of burn between the GAR and control groups ($p > 0.05$ for all). Scar sites were not significantly different between the groups ($p = 0.841$) (Table 1). The pre-training biomechanical properties of the burn scars and pre-training ROM of joints were not significantly different between the groups ($p > 0.05$ for all) (Table 2). None of the patients experienced skin abrasion around the burn scar when the fastening belts were applied

Table 3. Melanin, erythema and trans-epidermal water loss throughout the training regimen

Variable		Pre-training	At 4 weeks	At 12 weeks	P value
Melanin (AU)	GAR (<i>n</i> = 19)	163.9 ± 43.6	174.8 ± 43.7	192.4 ± 63.9	0.097 ^a
	Control (<i>n</i> = 20)	198.8 ± 77.0	185.9 ± 74.6	191.9 ± 68.8	0.786 ^a
Erythema (AU)	GAR (<i>n</i> = 19)	473.6 ± 85.0	498.3 ± 80.1	486.0 ± 77.5	0.570 ^a
	Control (<i>n</i> = 20)	455.5 ± 88.0	465.8 ± 87.1	447.9 ± 89.2	0.567 ^a
TEWL (g/h/m ²)	GAR (<i>n</i> = 19)	13.9 (12.1, 17.2)	15.9 (12.8, 18.8)	13.6 (12.3, 16.7)	0.766 ^b
	Control (<i>n</i> = 20)	15.7 (10.1, 17.8)	15.2 (12.8, 17.9)	15.2 (12.2, 16.6)	0.947 ^b

Data are presented as mean ± standard deviation or median (25% percentile, 75% percentile). GAR gait assistance robot, AU arbitrary unit, TEWL trans-epidermal water loss

^aOne way repeated-measures analysis of variance

^bFriedman test

Table 4. Comparison of skin biomechanical properties throughout the training regimen

Variable		Pre-training	At 4 weeks	At 12 weeks	P value
Thickness (mm)	GAR (<i>n</i> = 19)	1.86 ± 0.46	2.02 ± 0.50	2.11 ± 0.58	0.037 ^a
	Control (<i>n</i> = 20)	1.91 ± 0.51	2.02 ± 0.50	2.23 ± 0.63	0.019 ^a
Final distensibility (R0 = Uf)	GAR (<i>n</i> = 19)	0.54 (0.36, 1.74)	0.65 (0.40, 0.97)	0.68 (0.39, 0.86)	0.455 ^b
	Control (<i>n</i> = 20)	0.78 (0.33, 1.18)	0.65 (0.31, 1.11)	0.37 (0.23, 0.74)	0.011 ^b
Gross elasticity (R2 = Ua/Uf)	GAR (<i>n</i> = 19)	0.67 (0.03, 0.74)	0.74 (0.06, 0.80)	0.75 (0.11, 1.87)	0.873 ^b
	Control (<i>n</i> = 20)	0.61 (0.02, 0.73)	0.58 (0.09, 0.82)	0.52 (0.08, 0.80)	0.633 ^b
Viscoelasticity (R6 = Uv/Ue)	GAR (<i>n</i> = 19)	0.29 (0.01, 0.43)	0.31 (0.03, 0.49)	0.37 (0.02, 0.46)	0.559 ^b
	Control (<i>n</i> = 20)	0.34 (0.01, 0.47)	0.10 (0.03, 0.39)	0.21 (0.03, 0.38)	0.539 ^b
Hysteresis (R9 = H)	GAR (<i>n</i> = 19)	0.059 (0.033, 0.133)	0.059 (0.032, 0.122)	0.048 (0.022, 0.109)	0.038 ^b
	Control (<i>n</i> = 20)	0.065 (0.025, 0.125)	0.097 (0.031, 0.110)	0.101 (0.046, 0.1310)	0.804 ^b

Data are presented as mean ± standard deviation or median (25% percentile, 75% percentile). GAR gait assistance robot

^aOne way repeated-measures analysis of variance

^bFriedman test

Table 5. Comparison of change values in skin biomechanical properties between pre-training and 4 and 12 weeks after training

		GAR group	Control group	P value
Thickness (mm)	Pre ~4 wks	0.15 ± 0.30	0.12 ± 0.17	0.700 ^a
	Pre ~12 wks	0.12 ± 0.76	0.32 ± 0.55	0.337 ^a
Final distensibility (R0 = Uf)	Pre ~4 wks	-0.00 (-0.09, 0.00)	-0.04 (-0.37, 0.15)	0.297 ^b
	Pre ~12 wks	-0.13 (-0.67, 0.33)	-0.28 (-0.41, -0.01)	0.351 ^b
Gross elasticity (R2 = Ua/Uf)	Pre ~4 wks	0.00 (-0.01, 0.12)	0.03 (-0.01, 0.24)	0.820 ^b
	Pre ~12 wks	0.00 (-0.13, 0.23)	0.01 (-0.28, 0.14)	0.989 ^b
Viscoelasticity (R6 = Uv/Ue)	Pre ~4 wks	0.00 (-0.11, 0.07)	-0.01 (-0.31, 0.02)	0.653 ^b
	Pre ~12 wks	0.00 (-0.12, 0.08)	-0.01 (-0.33, 0.15)	0.569 ^b
Hysteresis (R9 = H)	Pre ~4 wks	0.003 (-0.019, 0.029)	-0.003 (-0.035, 0.032)	0.441 ^b
	Pre ~12 wks	-0.005 (-0.040, 0.005)	0.010 (-0.005, 0.043)	0.049 ^b

Data are presented as mean ± standard deviation or median (25% percentile, 75% percentile). GAR gait assistance robot, *wks* weeks

^aIndependent *t*-test

^bMann-Whitney *U* test

or musculoskeletal or cardiovascular adverse events, such as dizziness or changes in blood pressure, during training.

Table 3 shows the mean or median values of melanin, erythema and trans-epidermal water loss between the GAR and control groups before training and at 4 and 12 weeks after training. The levels of melanin, erythema and trans-epidermal water loss were not significantly different in both groups throughout the training regimen ($p > 0.05$ for all).

Scar thickness significantly increased in the GAR and control groups during the 12 weeks of training ($p = 0.037$ and $p = 0.019$, respectively). Final distensibility (R0) was not significantly different in the GAR group during training ($p = 0.455$) and significantly decreased in the control group during training ($p = 0.011$). There were no significant differences in the gross elasticity (R2) and viscoelasticity (R6) in both groups throughout the training regimen ($p = 0.873$ and

$p = 0.633$, and $p = 0.559$ and $p = 0.539$, respectively). Hysteresis (R9) was significantly reduced in the GAR group during the training ($p = 0.038$) and was not significantly different in the control group ($p = 0.804$) (Table 4).

The GAR and control groups showed significant difference in the change in the values of hysteresis (R9) between pre-training and 12 weeks after training ($p = 0.441$ and $p = 0.049$, respectively). Changes in values for scar thickness, distensibility (R0), gross elasticity (R2) and viscoelasticity (R6) were not significantly different between pre-training and 4 and 12 weeks after training ($p > 0.05$ for all) (Table 5).

Discussion

To the best of our knowledge, this is the first study to demonstrate the effects of RAGT-induced mechanical load on burn scars of the lower extremity. In our pilot study, three patients experienced skin abrasion on the burn scars when the fasten belt was applied at <2 months after injury. Therefore, we conducted RAGT at >2 months post-burn after the scars had become stable, and no patients experienced skin abrasion. Interestingly, RAGT-induced mechanical load significantly decreased the hysteresis of burn scars. Low hysteresis means less dissipation of energy during repetitive skin distension and relaxation [23] and indicates improvement in the tiring effect of skin [20].

Hypertrophic scars generally grow quickly from 3 to 6 months and can regress slightly after this period [24]. Since most of the burns in patients in this study were in the proliferative phase, both the GAR and control groups exhibited hypertrophic changes, with collagen and proteoglycan overproduction in the scars, and demonstrated a similar significant increase in scar thickness during training. Furthermore, no significant difference in scar thickness change was noted between the two groups. Aarabi et al reported that artificial mechanical loading in the early proliferative phase of wound healing induced hypertrophic scars by inhibiting apoptosis [12]. They applied mechanical stress earlier than in the GAR group and perpendicular to the craniocaudal axis. However, RAGT was conducted at >2 months after the burn injury and RAGT-induced mechanical load was applied parallel to the craniocaudal axis. These differences in the applied time and direction of mechanical stress could account for the inconsistencies with the findings of the previous study. Therefore, similar hypertrophic scar formation in the GAR and control groups is likely owing to chronic inflammation, cytokines, growth factors and macrophages associated with pathologic scar formation.

Collagen is the main component of the dermis (70–80% of the dry skin weight) that affects skin elasticity, and a proteoglycan-rich matrix is needed to maintain skin viscosity [25]. The overall viscoelasticity of the skin depends mainly on the connective tissue structure of the dermis and subcutaneous tissue, with minimal contribution from the epidermis [26]. The orientation, density, alignment and interconnections of collagen bundles also influence skin elasticity [27]. Stromal collagen is typically composed of type I and type III

collagen. Type I collagen fibres are thick and show minimal distensible activity when mechanical load is applied. Type III collagen bundles are thin and pliable and are enriched in the dermis, vasculature, internal organs and fine reticular fibres [28]. Hypertrophic scars demonstrated a low type I/III collagen ratio because they increased the expression of type III collagen and decreased the expression of type I collagen [29]. However, the predominant type III collagen bundles in hypertrophic scars are oriented parallel to the epithelial surface [30], compared to those in the normal dermis in which collagen bundles have a basket-weave pattern that permits tissue strength and flexibility [31]. Therefore, the parallel arrangement of the collagen bundles can make the scar less flexible and malleable [28] and decrease the distensibility in the scars, resulting from abnormal collagen patterns [30]. The skin distensibility of the burn scar significantly decreased in the control group during conventional training and this finding is consistent with those in previous studies [28,30]. However, the GAR group showed no significant change in skin distensibility during RAGT. Repetitive stretching of the human muscle–tendon units reduced peak passive tension and stiffness, and increased the utilization of elastic strain energy [32]. Therefore, improvement of the skin distensibility in the GAR group could be attributed to periodic and repetitive stretching exercises by the RAGT.

A force results in a certain change. Hysteresis refers to persistence of a condition or state even after the force is removed [33]. Hysteresis is represented in Figure S1 (see online supplementary material) by the area surrounded by the two curves that indicate the loading and unloading stages. When energy absorption and consumption are repeated during loading and unloading, more energy is absorbed at loading stress than at relaxation [34]. Hysteresis is also defined as the difference in energy changes in the tissue during loading and unloading in a stress–strain relationship [23], in which strain represents the ratio of altered to original tissue length [34]. The GAR group showed a decrease of hysteresis in hypertrophic burn scars after RAGT. Repetitive stretching significantly decreased hysteresis and stiffness of tendon structure [32]. Therefore, the reduced hysteresis in the hypertrophic scar of the GAR group could be attributed to periodic and repetitive stretching by RAGT.

Elastin is present in the dermis in small amounts (<1% of the dry skin weight) [35] and is involved in the initial elastic deformation of the stress–strain curve, as shown in Figure S1 [34]. Elastin, in particular, enables the collagen network to return to its original shape after stress removal [35]. Initial change of loading is mostly influenced by elastin fibres and after the initial stage, collagen fibres dominate deformation [36]. Elastin turnover is rare in healthy adult tissues because its half-life is ~70 years [37]. After stretching the scar tissue with a skin-stretching device, the alignment of the collagen bundle was more parallel than that of the nonstretched scars; however, the thickness and space of the collagen bundle were not significantly different between the stretched and nonstretched scars [38]. Additionally, the stretched scars showed no significant

difference in the quantity of elastic fibres compared with the nonstretched scars [38]. Therefore, the change in the scar biomechanical properties after RAGT could probably be explained by the realignment of the collagen bundle and interconnection of the connective tissue rather than any change in the elastin fibre.

The small sample size in this study may be a limitation on generalizing the results. Future *in vitro* and *in vivo* studies are warranted to demonstrate the mechanism of the effect of RAGT on the scar biomechanical properties and the distribution of collagen and elastin in scars after RAGT. RAGT could reduce personnel costs involved in manual assistance training [39]. Although the cost of rehabilitative therapy may not be uniform in each country, owing to the difference in the medical insurance systems, there is no difference in the cost between conventional training by a physical therapist and RAGT in South Korea. Since RAGT can reduce the time and labour required of a therapist for one patient, the cost and labour efficiencies are high [40,41]. Compared to the conventional training group, there was a better improvement in the isometric strength of the ankle and ROM of the knee and ankle in patients with burns after RAGT [2]. This study has the potential to clarify that RAGT does not negatively affect burn scars. Furthermore, it is expected to contribute to the active use of GAR in rehabilitation therapy for patients with burn injuries on the lower extremity.

Conclusions

In this study, RAGT significantly reduced hysteresis in hypertrophic burn scars and did not cause a significant decrease in skin distensibility, unlike in the control group. Furthermore, no skin complications were detected around the burn scars where the fastening belts were applied during RAGT.

Abbreviations

GAR: Gait assistance robot; RAGT: Robot-assisted gait training; ROM: Range of motion.

Supplementary data

Supplementary Material are available at *Burns & Trauma Journal* online.

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Authors' contributions

Conception and design: YSC, SYJ and CHS. Collection and assembly of data: YSC and SYJ. Data analysis and interpretation: YSC.

Manuscript writing: YSC. Revision of manuscript: SYJ and CHS. Final approval of manuscript: all authors.

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Ethical approval and consent to participate

The study and protocol were approved by the Institutional Review Board of Hangang Sacred Heart Hospital [HG2020-006] and are registered on the Clinical Research Information Service (KCT0005204).

Consent for publication

Consent for publication was obtained from the patients.

Conflicts of interest

None declared.

Data availability

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

References

1. Richard R, Santos-Lozada AR. Burn patient acuity demographics, scar contractures, and rehabilitation treatment time related to patient outcomes: the ACT study. *J Burn Care Res.* 2017;38:230–42.
2. Latarjet J, Choinère M. Pain in burn patients. *Burns.* 1995;21:344–8.
3. Joo SY, Lee SY, Cho YS, Lee KJ, Seo CH. Effects of robot-assisted gait training in patients with burn injury on lower extremity: a single-blind, randomized controlled trial. *J Clin Med.* 2020;9:2813.
4. Cen Y, Chai J, Chen H, Chen J, Guo G, Han C, *et al.* Guidelines for burn rehabilitation in China. *Burns Trauma.* 2015;3:20.
5. Esselman PC. Burn rehabilitation: an overview. *Arch Phys Med Rehabil.* 2007;88:S3–6.
6. Van Peppen RP, Kwakkel G, Wood-Dauphinee S, Hendriks HJ, Van Der Wees PJ, Dekker J. The impact of physical therapy on functional outcomes after stroke: what's the evidence? *Clin Rehabil.* 2004;18:833–62.
7. Richards CL, Malouin F, Wood-Dauphinee S, Williams JL, Bouchard JP, Brunet D. Task-specific physical therapy for optimization of gait recovery in acute stroke patients. *Arch Phys Med Rehabil.* 1993;74:612–20.
8. Nilsson A, Vreede KS, Häglund V, Dawamoto H, Sankai Y, Borg J. Gait training early after stroke with a new exoskeleton – the hybrid assistive limb: a study of safety and feasibility. *J Neuroeng Rehabil.* 2014;11:92.
9. Galli M, Cimolin V, De Pandis MF, Le Pera D, Sova I, Albertini G, *et al.* Robot-assisted gait training versus treadmill training in patients with Parkinson's disease: a kinematic evaluation with gait profile score. *Funct Neurol.* 2016;31:163–70.

10. Tanaka Y, Oka H, Nakayama S, Ueno T, Matsudaira K, Miura T, *et al.* Improvement of walking ability during postoperative rehabilitation with the hybrid assistive limb after total knee arthroplasty: a randomized controlled study. *SAGE Open Med.* 2017;5:2050312117712888. <https://doi.org/10.1177/2050312117712888>.
11. Joo SY, Lee SY, Cho YS, Lee KJ, Kim SH, Seo CH. Effectiveness of robot-assisted gait training on patients with burns: a preliminary study. *Comput Methods Biomech Biomed Engin.* 2020;23:888–93.
12. Aarabi S, Bhatt KA, Shi Y, Paterno J, Chang EI, Loh SA, *et al.* Mechanical load initiates hypertrophic scar formation through decreased cellular apoptosis. *FASEB J.* 2007;21:3250–61.
13. Kolpakov V, Rekhter MD, Gordon D, Wang WH, Kulik TJ. Effect of mechanical forces on growth and matrix protein synthesis in the in vitro pulmonary artery. Analysis of the role of individual cell types. *Circ Res.* 1995;77:823–31.
14. Maggioni S, Melendez-Calderon A, Van Asseldonk E, Klamroth-Marganska V, Lünenburger L, Riener R, *et al.* Robot-aided assessment of lower extremity functions: a review. *J Neuroeng Rehabil.* 2016;13:72.
15. Nedelec B, Correa JA, de Oliveira A, LaSalle L, Perrault I. Longitudinal burn scar quantification. *Burns.* 2014;40:1504–12.
16. Nedelec B, Correa JA, Rachelska G, Armour A, LaSalle L. Quantitative measurement of hypertrophic scar: intrarater reliability, sensitivity, and specificity. *J Burn Care Res.* 2008;29:489–500.
17. Park JW, Seo CH, Han SH, Lee YG. Sympathetic influence on biomechanical skin properties after spinal cord injury. *Spinal Cord.* 2011;49:236–43.
18. Ryu HS, Joo YH, Kim SO, Park KC, Youn SW. Influence of age and regional differences on skin elasticity as measured by the Cutometer®. *Skin Res Technol.* 2008;14:354–8.
19. Nguyen DQ, Potokar TS, Price P. An objective long-term evaluation of Integra (a dermal skin substitute) and split thickness skin grafts, in acute burns and reconstructive surgery. *Burns.* 2010;36:23–8.
20. Dobrev H. In vivo study of skin mechanical properties in psoriasis vulgaris. *Acta Derm Venereol.* 2000;80:263–6.
21. Cho YS, Lee J, Joo SY, Seo CH. Crosstalk among adipose tissue, vitamin D level, and biomechanical properties of hypertrophic burn scars. *Burns.* 2019;45:1430–7.
22. Cunningham JB, McCrum-Gardner E. Power, effect and sample size using GPower: practical issues for researchers and members of research ethics committees. *Evidence-Based Midwifery.* 2007;5:132–7.
23. Wiśniewska A, Liber-Kneć A. Influence of a skin tissue anisotropy on mechanical hysteresis. *Technical Transactions/Czasopismo Techniczne.* 2016;15:125–36.
24. Trisiliana Perdanasari A, Torresetti M, Grassetti L, Nicoli F, Zhang YX, Dashti T, *et al.* Intralesional injection treatment of hypertrophic scars and keloids: a systematic review regarding outcomes. *Burns Trauma.* 2015;3:14.
25. Daly CH. Biomechanical properties of dermis. *J Invest Dermatol.* 1982;79:17–20.
26. Henry F, Goffin V, Piérard-Franchimont C, Piérard GE. Mechanical properties of skin in Ehlers-Danlos syndrome, types I, II, and III. *Pediatr Dermatol.* 1996;13:464–7.
27. Piérard GE, Piérard-Franchimont C, Vanderplaetsen S, Franchimont N, Gaspard U, Malaise M. Relationship between bone mass density and tensile strength of the skin in women. *Eur J Clin Invest.* 2001;31:731–5.
28. Ehrlich HP. Collagen considerations in scarring and regenerative repair. In: Garg HG, Longaker MT. (eds.). *Scarless wound healing*. CRC Press: Boca Raton, FL, USA, 2000, 99–113.
29. Finnerty CC, Jeschke MG, Branski LK, Barret JP, Dziewulski P, Herndon DN. Hypertrophic scarring: the greatest unmet challenge after burn injury. *Lancet.* 2016;388:1427–36.
30. Linares HA. From wound to scar. *Burns.* 1996;22:339–52.
31. Zhu Z, Ding J, Tredget EE. The molecular basis of hypertrophic scars. *Burns Trauma.* 2016;4:2.
32. Kubo K, Kanehisa H, Kawakami Y, Fukunaga T. Influence of static stretching on viscoelastic properties of human tendon structures in vivo. *J Appl Physiol.* 2001;90:520–7.
33. Mizuno K, Boudko SP, Engel J, Bächinger HP. Kinetic hysteresis in collagen folding. *Biophys J.* 2010;98:3004–14.
34. Piérard GE, Piérard S, Delvenne P, Piérard-Franchimont C. In vivo evaluation of the skin tensile strength by the suction method: pilot study coping with hysteresis and creep extension. *ISRN Dermatol.* 2013;2013:841217. <https://doi.org/10.1155/2013/841217>.
35. Solan A, Dahl SL, Niklason LE. Effects of mechanical stretch on collagen and cross-linking in engineered blood vessels. *Cell Transplant.* 2009;18:915–21.
36. Hussain SH, Limthongkul B, Humphreys TR. The biomechanical properties of the skin. *Dermato Surg.* 2013;39:193–203.
37. Uitto VJ, Larjava H. Extracellular matrix molecules and their receptors: an overview with special emphasis on periodontal tissues. *Crit Rev Oral Biol Med.* 1991;2:323–54.
38. Verhaegen PD, Schouten HJ, Tigchelaar-Gutter W, van Marle J, van Noorden CJ, Middelkoop E, *et al.* Adaptation of the dermal collagen structure of human skin and scar tissue in response to stretch: an experimental study. *Wound Repair Regen.* 2012;20:658–66.
39. Nam KY, Kim HJ, Kwon BS, Park JW, Lee HJ, Yoo A. Robot-assisted gait training (Lokomat) improves walking function and activity in people with spinal cord injury: a systematic review. *J Neuroeng Rehabil.* 2017;14:1–13.
40. Chang MC, Chun MH. Use of robots in rehabilitative treatment. *K Korean Med Assoc.* 2015;58:141–6.
41. Yang X, Li GH, Wang HJ, Wang CY. Continuous passive motion after total knee arthroplasty: a systematic review and meta-analysis of associated effects on clinical outcomes. *Arch Phys Med Rehabil.* 2019;100:1763–78.