

Evaluating the efficacy of portable air-fed cold atmospheric plasma device for alleviating burn hypertrophic scar and neuropathic pain

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Abstract

Background: Burn-induced hypertrophic scars are associated with excessive fibrosis, tissue stiffness, and mechanical hypersensitivity. This study evaluated the therapeutic efficacy and systemic safety of a portable air-fed cold atmospheric plasma (CAP) device.

Methods: Hypertrophic scars were established on the hind paws of Sprague–Dawley rats. After wound closure, rats received no treatment or CAP for 4 or 8 minutes, three times weekly for six weeks. Scar appearance, firmness, paw withdrawal threshold, histology, and serum biochemical markers were evaluated.

Results: Both CAP regimens reduced scar firmness, thickness, and Scar Elevation Index after 6 weeks treatment and increased paw withdrawal thresholds from Week 4 onward. CAP treatment increased ALT but did not significantly alter AST, BUN, or creatinine.

Conclusion: Portable air-fed CAP may provide a non-invasive treatment for burn hypertrophic scars and associated mechanical hypersensitivity.

Introduction

- Hypertrophic scars develop in up to 70% of patients following deep burns. Persistent inflammation and excessive extracellular matrix deposition contribute to scar thickening, stiffness, mechanical hypersensitivity, and neuropathic pain. Current treatments have variable efficacy and may be limited by discomfort, recurrence, and poor adherence.
- CAP generates bioactive reactive oxygen and nitrogen species. Preliminary in vitro evidence suggests that CAP may modulate cellular responses associated with inflammation and fibrosis. However, these potential effects haven’t been sufficiently evaluated in vivo, particularly in established burn hypertrophic scars. Previous CAP research has primarily focused on disinfection and acute wound healing, leaving its effects during the scar-remodeling phase and on scar-associated mechanical hypersensitivity largely unexplored.

Objective: To evaluate the efficacy and systemic safety of portable air-fed CAP for treating burn-induced hypertrophic scars and mechanical hypersensitivity.

Methods

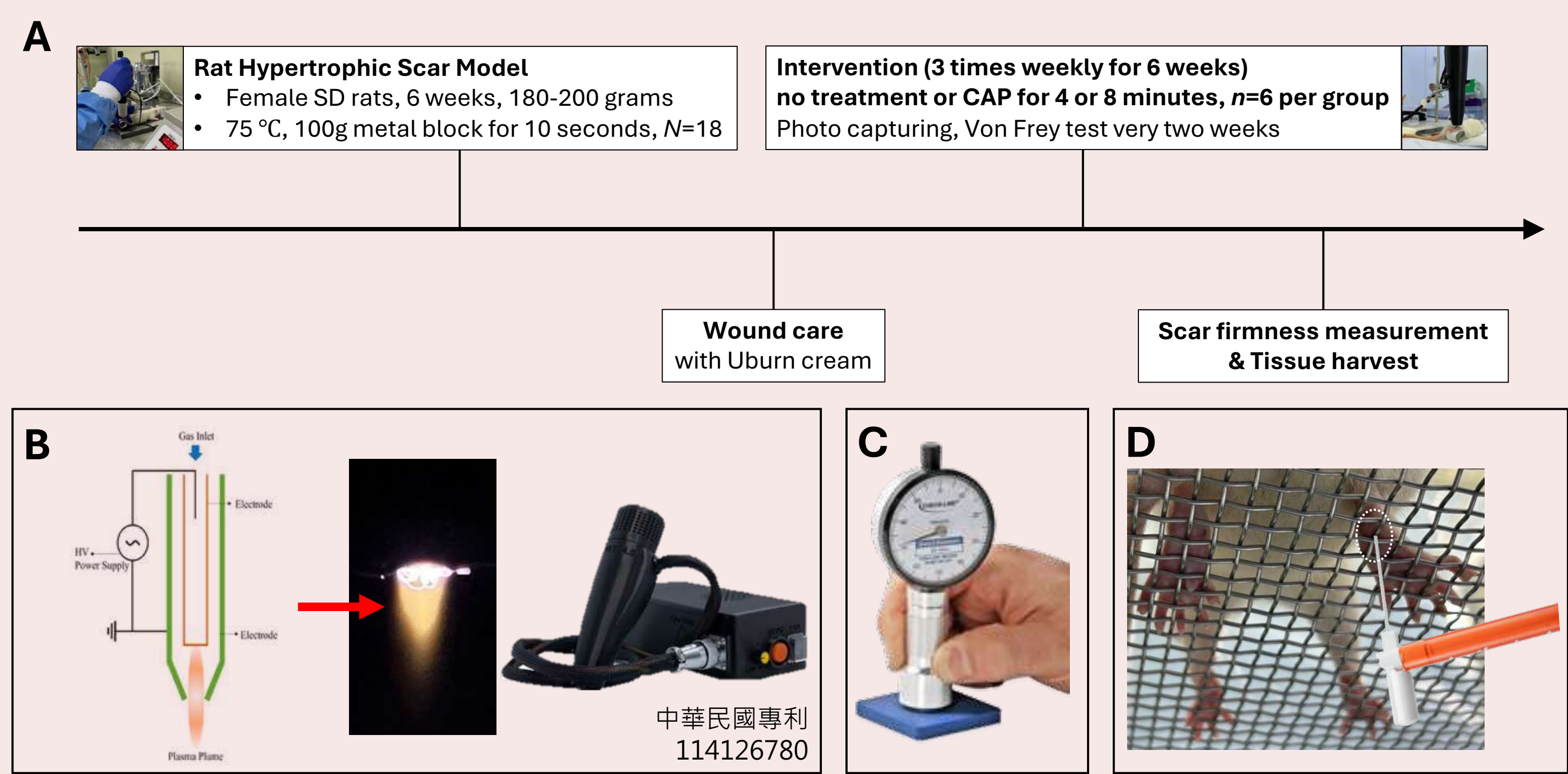


Figure 1. Experimental design, CAP device, and outcome measurements. (A) A burn injury was induced on the plantar surface of the hind paw of female Sprague–Dawley rats using a 100-g metal block heated to 75°C for 10 seconds. After wound closure and scar formation, rats were assigned to an untreated burn control group or received CAP treatment for 4 or 8 minutes, three times weekly for six weeks ($n = 6$ per group). (B) Schematic, plasma plume, and portable air-fed atmospheric-pressure plasma jet (APPJ) developed and provided by Prof. Yu-Lin Kuo’s laboratory at National Taiwan University of Science and Technology. The APPJ was operated at 4.44 kV, 15 mA, and 28.2 kHz, with a nozzle-to-tissue distance of 0.5 cm and a treatment temperature below 35°C. (C) Scar firmness was measured using a Shore OO durometer. (D) Mechanical paw withdrawal threshold was assessed by applying von Frey filaments to the center of the plantar scar.

Results

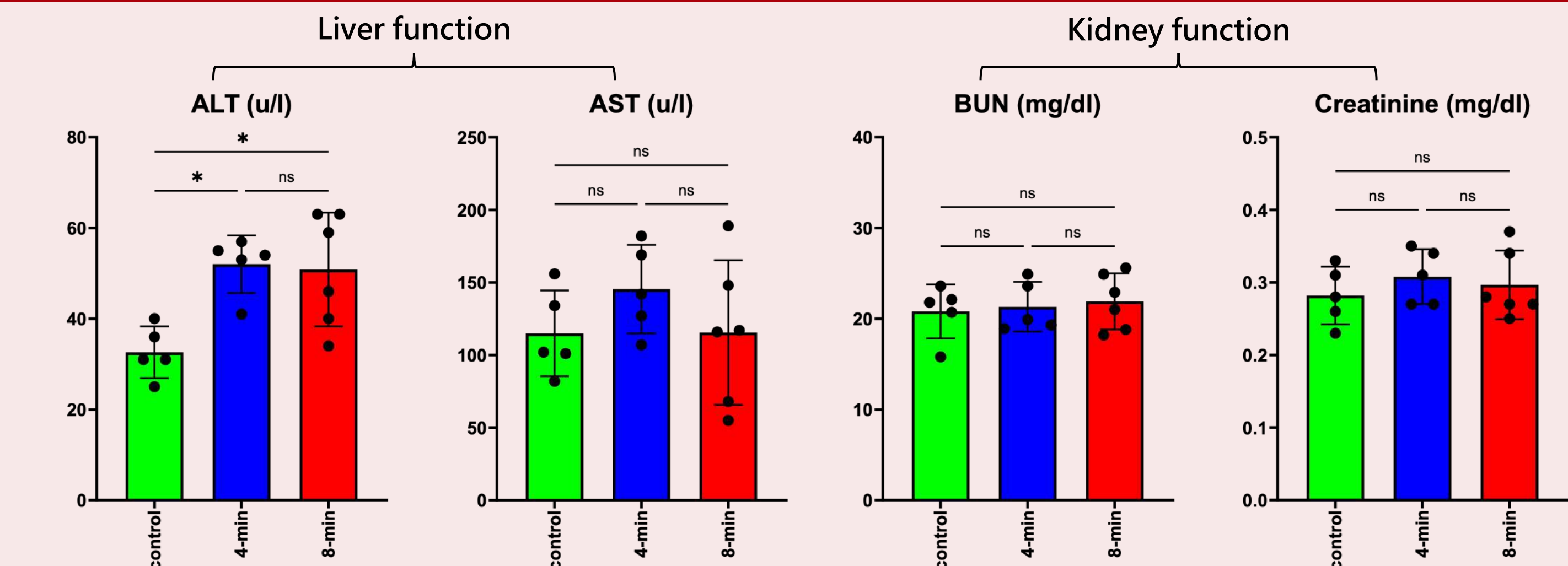


Figure 2. Serum biochemical parameters following repeated CAP treatment. Serum levels of (A) alanine aminotransferase (ALT), (B) aspartate aminotransferase (AST), (C) blood urea nitrogen (BUN), and (D) creatinine were measured after six weeks of treatment. ALT levels were significantly higher in both CAP-treated groups than in the untreated burn control group, whereas no significant difference was observed between the 4- and 8-minute regimens. No significant differences in AST, BUN, or creatinine were observed among the three groups. The absence of treatment-related changes in AST, BUN, and creatinine suggests no detectable alteration in these measured hepatic and renal biochemical parameters.

Results

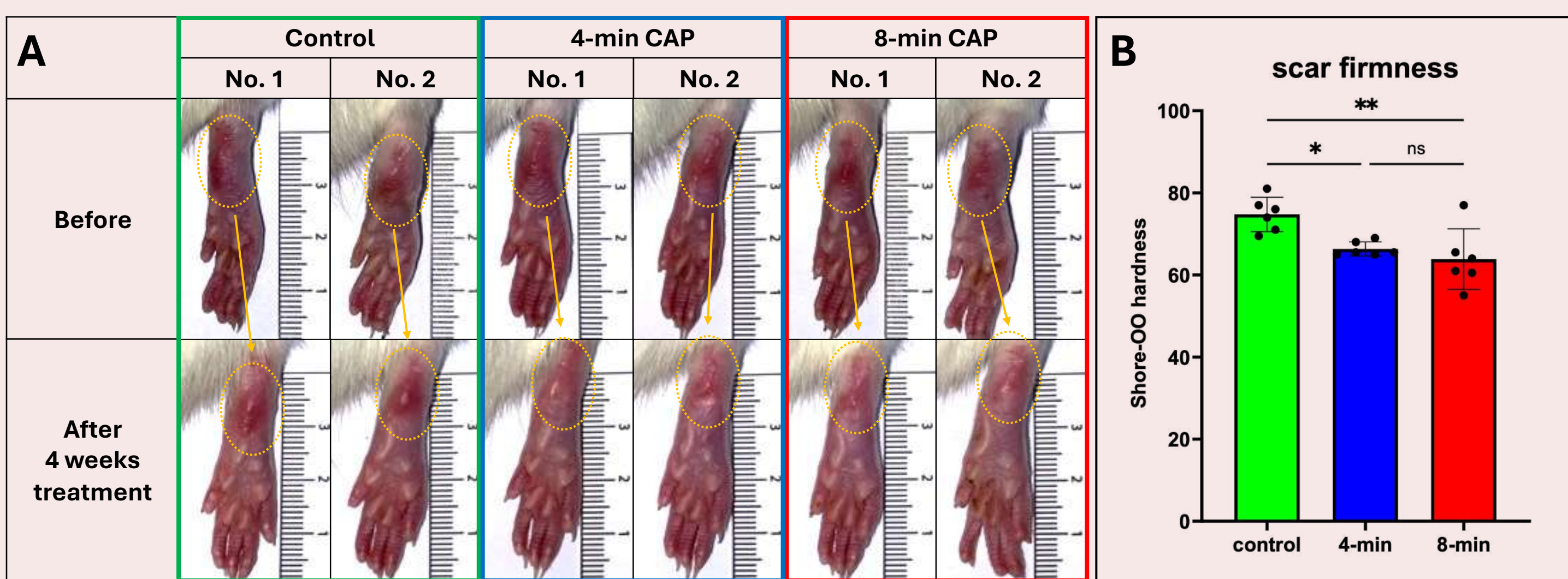


Figure 3. CAP treatment improved the macroscopic appearance and reduced the firmness of burn-induced hypertrophic scars. (A) Representative photographs of the hind-paw scars before treatment and after four weeks of intervention. Compared with the untreated burn control group, both the 4-minute and 8-minute CAP groups showed visually reduced scar erythema and swelling after four weeks of treatment. (B) Scar firmness measured using a Shore-OO durometer after six weeks of treatment. Both CAP-treated groups exhibited significantly lower scar firmness than the untreated burn control group, with no significant difference between the two CAP treatment durations.

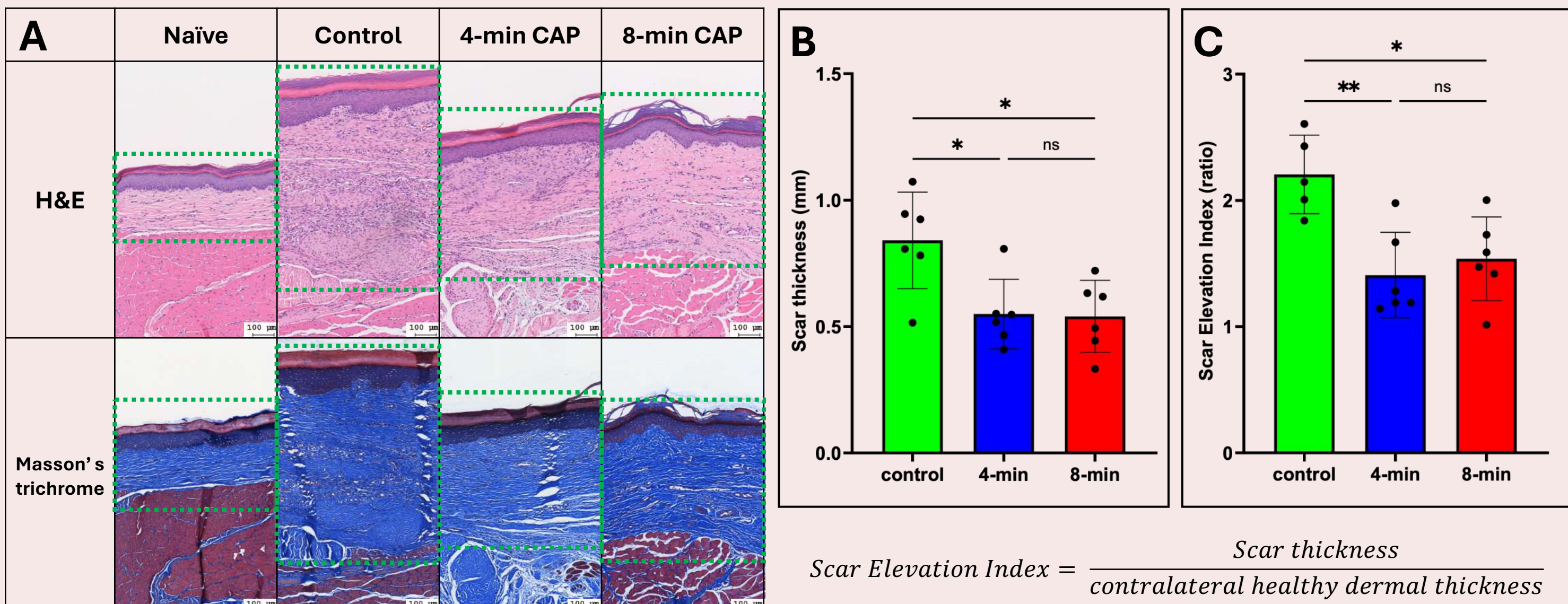


Figure 4. CAP treatment improved hypertrophic scar histology. Representative (A) H&E and Masson’s trichrome staining showed reduced scar thickness and improved collagen organization after CAP treatment. Both CAP regimens significantly reduced (B) total scar thickness and (C) Scar Elevation Index, with no significant difference between treatment durations. SEI was normalized to the corresponding dermal thickness of the contralateral healthy hind paw.

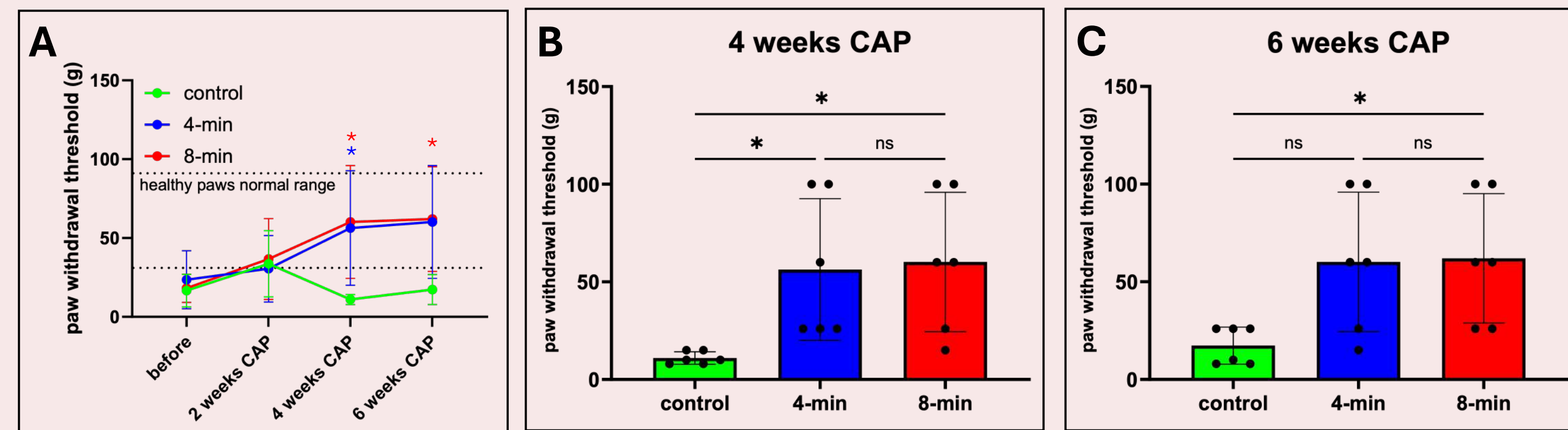


Figure 5. CAP treatment attenuated burn-induced mechanical hypersensitivity. (A) Mechanical paw withdrawal threshold (PWT) was assessed longitudinally using von Frey filaments during the six-week treatment period. All groups exhibited similarly low baseline PWTs before treatment. PWT progressively increased in both CAP-treated groups, whereas the untreated burn control group remained low after Week 4. (B) At Week 4, PWT was significantly higher in both the 4-minute and 8-minute CAP groups than in the untreated burn control group. (C) At Week 6, PWT remained significantly higher in the 8-minute CAP group than in the untreated burn control group, while the 4-minute group showed a similar increase that did not reach statistical significance. No significant difference was observed between the two CAP treatment durations.

Discussion

- Portable air-fed CAP improved the biomechanical and histological features of established burn hypertrophic scars.
- CAP progressively increased paw withdrawal thresholds, indicating attenuation of burn-induced mechanical hypersensitivity.
- The 4-minute CAP regimen achieved effects comparable to those of the 8-minute regimen, supporting the use of the shorter treatment duration.
- AST, BUN, and creatinine were not significantly altered, while the isolated ALT elevation requires further investigation.
- Future studies will investigate fibrosis-related signaling pathways in scar tissue and neuropathic pain-associated neuroinflammatory signaling in the dorsal root ganglia to clarify the mechanisms of CAP treatment using immunohistochemistry, western blotting, and RNA-seq.

Acknowledgements

