# Randomized Controlled Study of Immune Mechanisms of Vitamin D to Reduce Chronic Pain After Thermal Burn Injury

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## INTRODUCTION

- Burn injuries affect 11 million people annually worldwide.
- Chronic pain is a common, morbid sequelae of burn injury.
- Low vitamin D is associated with several chronic pain conditions and vitamin D has improved pain outcomes for inflammatory disorders.
- Vitamin D deficiency is common in patients with burn injuries.
- Observational studies have shown that low vitamin at the time of a burn injury is associated with greater chronic pain.
- We hypothesize that vitamin D reduces chronic pain after a burn injury by an immune mechanism.
- We hypothesize that vitamin D is an anti-inflammatory that reduces pro-inflammatory cells and increases anti-inflammatory cells. We also predict that vitamin D decreases toll-like receptor 4 activation.
- To assess the mechanism of vitamin D and determine the feasibility of a one-time dose strategy, we are conducting a follow-up pilot RCT.

## METHODS

- This pilot, double-blind, randomized controlled trial enrolls adult patients who present to UNC Hospitals within 1 week of major thermal burn injury (MThBI).
- Only individuals with total body surface area burned ≤30% are enrolled.
- Before study drug administration, Vitamin D levels are measured using a finger-prick test to prevent toxic levels.
- Patients are administered a one-time dose of vitamin D (300,000 IU) or placebo at enrollment.
- Pain severity and psychological and social interference are assessed at enrollment, 6 weeks, 3 months and 6 months after MThBI via structured in-person interviews and online surveys.
- 1, 25(OH) Vitamin D levels are determined from plasma obtained within 1 week following MThBI and at 6 weeks.
- Immune mechanisms will be assessed using single-cell mass cytometry using blood samples collected as enrollment and 6 weeks.

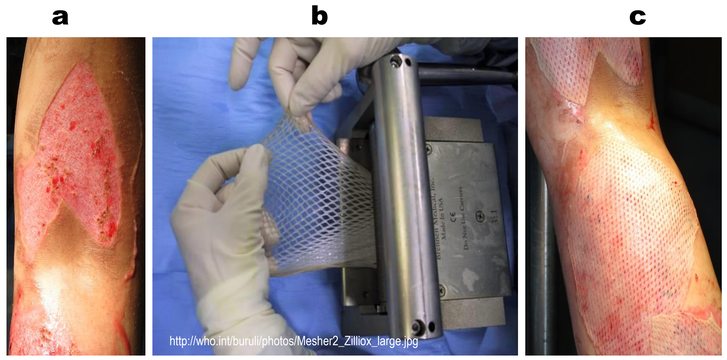


**Figure 1: Skin graft procedure for coverage of burn injury site.** Figure 1a shows the burn injury site after debridement. Figure 1b shows the process in which harvested skin from a donor site is meshed with a microtome to provide more extensive coverage of the burn injury site. Figure 1c shows a burn injury site covered with meshed tissue autograft.

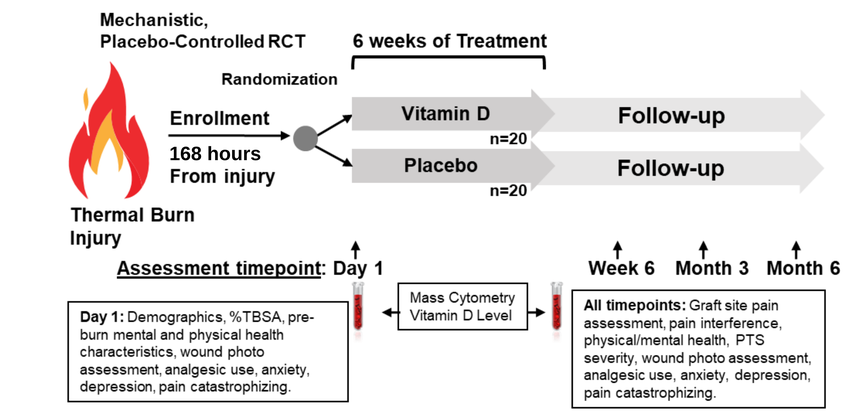


**Figure 2: General Design Overview** Patients are admitted to hospital and administered vit D or placebo within one week of burn injury. Blood samples from enrollment and 6 weeks used to assess vit D changes and evaluate mechanisms. Patients complete assessments at enrollment, week 6, and months 3 and 6.

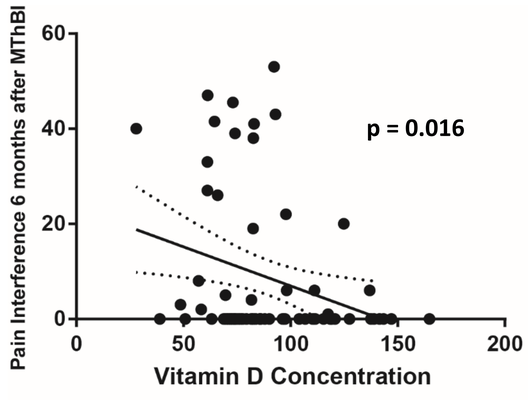


**Figure 3: Low Vitamin D concentration early after injury predicts chronic pain severity 6 months following MThBI.** Patients with low levels of Vitamin D in the early aftermath of MThBI have greater chronic pain severity 6 months after injury.

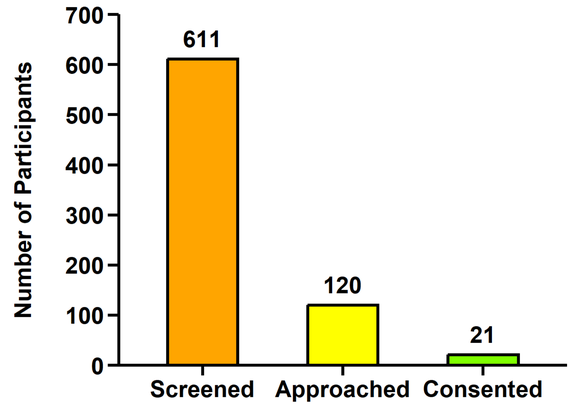


**Figure 4: Enrollment Progress as of March 2024** Of the 611 patients screened, 120 (19.6%) patients were eligible based on medical review and were approached for enrollment, 21 (17.5% of whom were ultimately enrolled and consented.

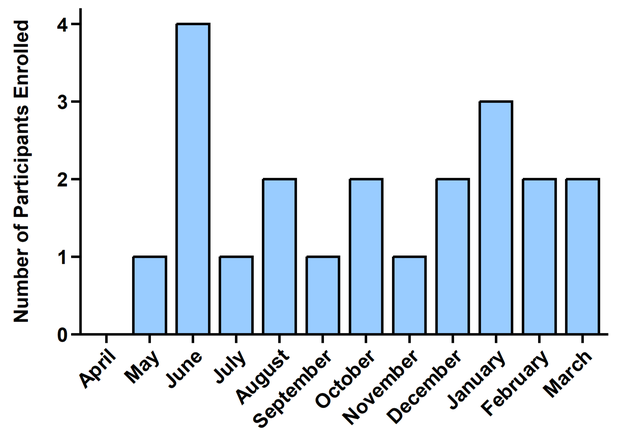


**Figure 5: Monthly Enrollment From April 2023- March 2024** A total of 21 patients have been enrolled, with the most in a month being 4 patients and the least 0 patients. On average, ~2 patients are enrolled per month.

## REFERENCES


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