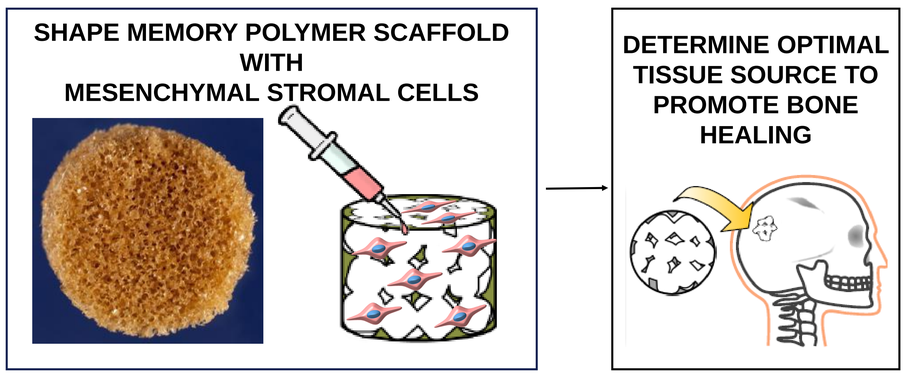
Combat and trauma can result in massive bone loss, which pose significant challenges to healing. Autografting remains the gold standard of treatment for critical size defects; however, risks include donor site morbidity and limited availability. An alternative is allografts but they are suboptimal as they have reduced osteo-inductive capabilities. We propose a cell/biomaterial-based therapy to improve bone healing with adipose (ADSC), bone marrow (BMSC), or umbilical cord (UCSC) derived human mesenchymal stromal cells (MSCs) in a novel poly(ε-caprolactone) shape memory polymer (SMP) scaffold coated with polydopamine. The benefits of this scaffold include the ability to custom fit into irregularly shaped defects and a slow degradation profile that supports bone growth. This study aims to determine if MSCs are most effective in their pre-differentiated or undifferentiated state and compare the cell source with a novel SMP scaffold.

METHODS

- **Cell Culture:** MSCs (Promocell) were cultured in growth or differentiation medium at 37°C/5% CO_2. The scaffold was incorporated ADSCs, BMSCs, or UCSCs in their undifferentiated state or pre-differentiated towards osteoblasts.
- **Bone Defect:** An 8mm calvarial defect was created in male RNU (Crl: NIH-*Fox1*^{rnu}) rats (250-300g) between the bregma and lamboid suture. Rats were randomized to the following groups.
  - No scaffold (defect only)
  - Scaffold without cells (scaffold only)
  - Scaffold with undifferentiated MSCs
  - Scaffold with pre-differentiated MSCs
- Bone healing was evaluated at 4 and 12 weeks.
  - **Push-out Test:** The scaffold was pushed out of the defect site with an Instron device to determine the maximum force (n=8).
  - **MicroCT:** New bone formation was determined via microCT with a Skyskan 1172 and analyzed with Skyscan CTAn software (n=8).
- **Statistics:** A one-way ANOVA for each time point was run for undifferentiated and pre-differentiated MSCs on log transformed data with a Tukey's post-hoc test.



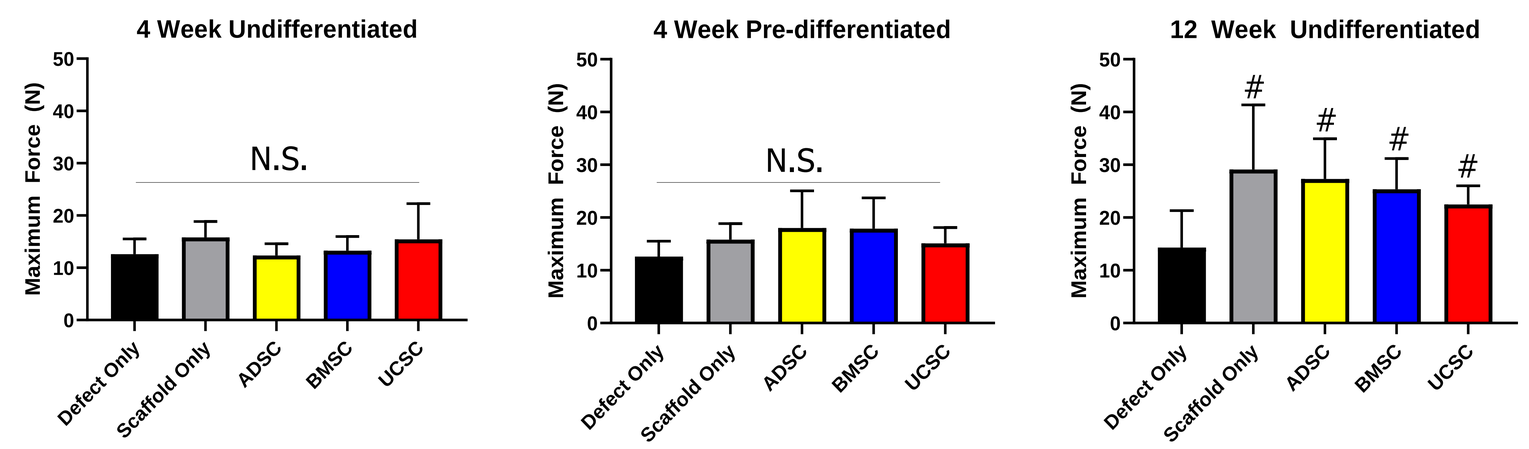


Figure 1. Push-out test. Osseointegration increased at 12 weeks for groups con Increased maximum force from the defect only group within each graph is noted by # (p<

RESULTS: NEW BONE GROWTH AND STRUCTUR

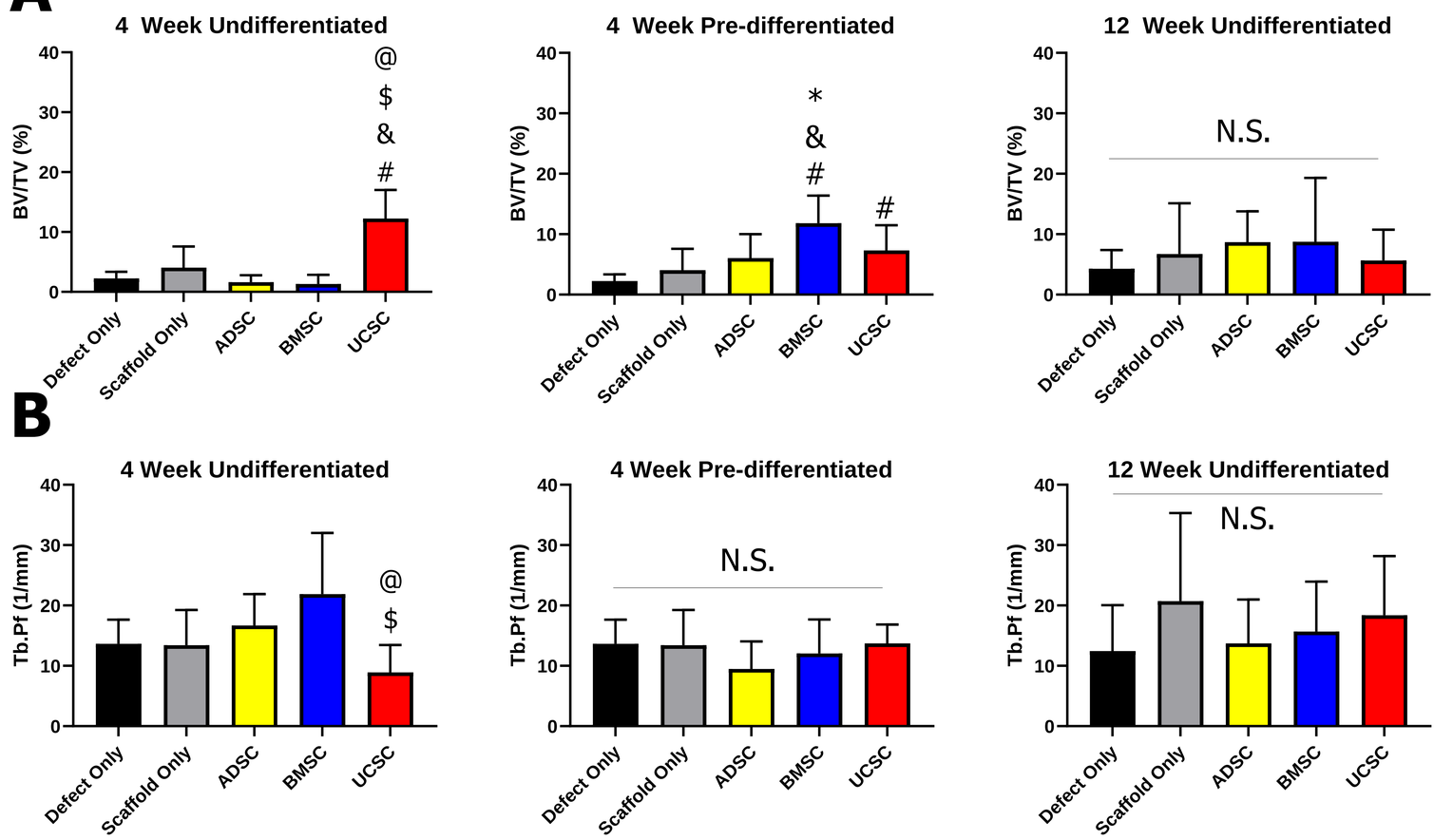


Figure 2. MicroCT. New bone formation and structure was determined via microCT. (A to tissue volume (BV/TV) was compared to determine new bone formation. (B) Trabec incorporates trabecular number, spacing, and thickness with a lower Tb.Pf indicating Statistical differences are reported within each graph as (#) different than defect only, only, ($) different than ADSC, and (@) different than BMSC (p<0.05).

CONCLUSIONS

- The SMP scaffold, with or without MSCs, increased the maximum force to push the scaffold out of the defect site after 12 weeks of healing.
- Pre-differentiated ADSC, BMSC, and UCSC had more new bone formation than the controls after 12 weeks. The data suggests pre-differentiated MSCs contributed to more healing than their undifferentiated counterpart.
- Pre-differentiated ADSC had the most mature bone compared to scaffold only after 12 weeks.
- Overall, there were few differences between MSC tissue sources.
- Further analysis will include histological analysis of the defect area to examine bone integration throughout the SMP scaffold.

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