Intradiscal Injections of Autologous Bone Marrow Aspirate Concentrate Increase Disc Hydration and Reduce Patient Reported Disability and Pain

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Introduction: Intradiscal injections of autologous bone marrow aspirate concentrate (BMAC) have emerged as a promising treatment for intervertebral disc (IVD) degeneration. This minimally invasive procedure circumvents the need for viable cell donors by using a patient's own cells, anti-inflammatory cytokines, and growth factors when treating a degenerative disc. As such, recent studies have demonstrated that BMAC injections led to a sustained reduction in patient reported pain and disability, making this treatment an attractive candidate for halting the progression of disc disease[1,2]. Although this treatment holds great promise, the mechanism behind these improvements remains unclear. Moreover, little is known on how BMAC injections affect the composition or structure of treated discs. We have previously documented changes in disc hydration and nucleus pulposus (NP) size via T2 mapping in several animal models[3,4]. However, no present study has evaluated the effect of BMAC injections on changes in human disc hydration and NP size. In this study, we evaluated the long-term effects of BMAC treatment on IVD composition, structure, and patient reported outcomes, hypothesizing that BMAC injections would lead to improvements in T2 intensity, NP size, patient reported disability, and pain.

Methods: *Patient recruitment*: All human studies were in accordance with our institutional review board. Patients were selected based on the following inclusion criteria: Subjects must be at least 18 years old with radiologically confirmed diagnosis of degenerative disc disease in the lumbar spine. Subjects must also be unresponsive to conservative/non-operative treatments for more than 3 months. *Imaging and quantification*: T2 MRI scans were taken of patients pre-op, 3 months post-op, and 1 year post-op to quantify changes in disc hydration and NP size (n=5 patients, n=15 discs). Treated IVDs were segmented from surrounding tissues by applying a Gaussian mixture model to first-echo T2 images and T2 maps as previously described[3]. Histograms of T2 intensities for each disc were fit to two normal distributions, one for background tissue and one for disc tissue. Each disc was manually segmented from any background tissue by applying a threshold 2-5 standard deviations from the center of the background peak **(Fig. 1)**. Once IVDs were segmented, average T2 intensities and NP sizes were calculated from remaining voxels. The mean T2 relaxation time and NP size of treated discs were normalized to adjacent healthy controls. *Patient reported outcome measures (PROMs):* Recruited subjects filled out a low back pain questionnaire and a pain assessment survey to determine Oswestry Disability Index (ODI) and Numeric Rating Scale (NRS) scores, respectively. ODI, NRS leg, and NRS back scores were recorded pre-op, 3 months post-op, 6 months post-op, and 1 year post-op (n=22 patients, n=264 measurements). *Statistics*: Changes in T2 relaxation time and NP size were analyzed using a repeated measures one-way ANOVA. Changes in ODI and NRS scores were analyzed using a one-way ANOVA.

Results: Quantitative T2 mapping revealed that BMAC injections led to a significant increase in T2 relaxation time ($P<0.05$), indicating increased water content in treated discs **(Fig. 2)**. Moreover, BMAC treated discs trended towards an increase in NP size, with 3 patients demonstrating an increase in NP size and 2 patients demonstrating a decrease **(Fig. 2)**. Patient disability questionnaires demonstrated that BMAC injections led to a significant decrease ODI scores over time ($P<0.0001$) **(Fig. 3)**. Patient pain questionnaires revealed that BMAC injections led to a significant decrease NRS leg and NRS back scores over time ($P<0.0001$) **(Fig. 3)**.

Discussion: In this study, we found that intradiscal injections of autologous BMAC improved disc hydration after 1 year. Additionally, BMAC treated discs trended towards an increase in NP size over time. Variations in treatment response may be explained by differences in the composition of injected aspirates. Several studies have demonstrated that bone marrow-derived mesenchymal stem or stromal cells (MSCs) are key regulators of tissue repair and regeneration[5]. However, injected cells have a short residence time in the disc[6,7]. This suggests that improvements in T2 intensity and NP size are linked to paracrine signaling from MSCs rather than the prolonged presence of MSCs in the disc. BMAC injections led to a sustained reduction in ODI, NRS leg, and NRS back scores, implicating the therapeutic benefit of this procedure. These improvements in disability and pain metrics are consistent with results from similar trials, yielding over a 50% improvement in patient reported outcomes[1,2]. Our work confirms that BMAC injections lead to compositional, structural, disability, and pain related changes in treated discs by improving disc hydration, reducing patient reported pain and disability, and trending towards an increase in NP size.

Significance: Intradiscal injections of autologous BMAC lead to long-term improvements in disc health and patient reported outcomes, demonstrating the effects of this treatment on IVD composition and structure, and highlighting the potential of BMAC as a bioactive therapeutic for disc degeneration.

References: 1. Haines+ 2022, 2. Wolff+ 2020, 3. Hussain+ 2019, 4. Grunert+ 2015, 5. Hu+ 2022, 6. Oehme+ 2015, 7. Vadala+ 2012

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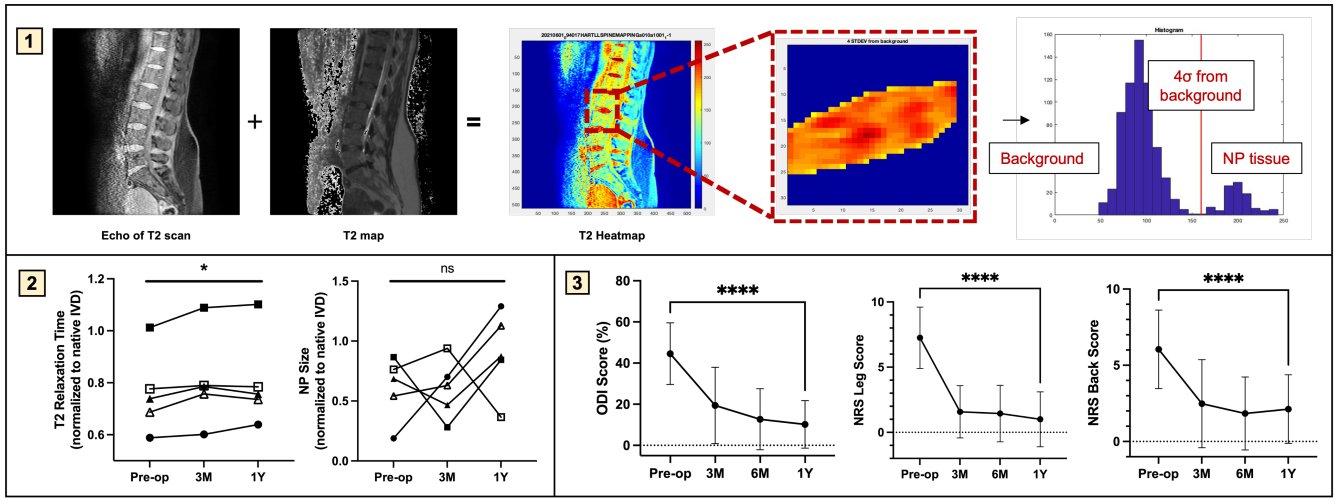

Figure 1: Left) Methodology for quantitative T2 mapping from human MRI scans. Right) Histogram of T2 intensities fit to a Gaussian mixture model.
Figure 2: Left) T2 relaxation times of BMAC treated discs over time normalized to native IVD. Right) NP size measurements of BMAC treated discs over time normalized to native IVD.
Figure 3: Left) ODI scores of BMAC treated patients over time. Mid) NRS leg scores of BMAC treated patients over time. Right) NRS back scores of BMAC treated patients over time.