## Gender Specific Differences in Clinical Outcomes of Knee Osteoarthritis Treated with Micro-Fragmented Adipose Tissue

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Abstract : Knee Osteoarthritis (OA) is a critical cause of disability globally. In recent years, there has been growing interest in non-invasive treatments, such as intra-articular injection of micro-fragmented fat (MFAT), showing great potential in treating OA. Mesenchymal stem cells (MSCs), originating from pericytes of micro-vessels in MFAT, can differentiate into mesenchymal lineage cells such as cartilage, osteocytes, adipocytes, and osteoblasts. Secretion of growth factor and cytokines from MSCs have the capability to inhibit T cell growth, reduced pain and inflammation, and create a micro-environment that through paracrine signaling, can promote joint repair and cartilage regeneration. Here we have shown, for the first time, data supporting the hypothesis that women respond better in terms of improvements in pain and function to MFAT injection compared to men. Historically, women have been underrepresented in studies, and studies with both sexes regularly fail to analyse the results by sex. To mitigate this bias and quantify it, we describe a technique using reproducible statistical analysis and replicable results with Open Access statistical software R to calculate the magnitude of this difference. Genetic, hormonal, environmental, and age factors play a role in our observed difference between the sexes. This observational, intention-to-treat study included the complete sample of 456 patients who agreed to be scored for pain (visual analogue scale (VAS)) and function (Oxford knee score (OKS)) at baseline regardless of subsequent changes to adherence or status during follow-up. We report that a significantly larger number of women responded to treatment than men: [90% vs. 60% change in VAS scores with 87% vs. 65% change in OKS scores, respectively]. Women overall had a stronger positive response to treatment with reduced pain and improved mobility and function. Pre-injection, our cohort of women were in more pain with worse joint function which is quite common to see in orthopaedics. However, during the 2-year follow-up, they consistently maintained a lower incidence of discomfort with superior joint function. This data clearly identifies a clear need for further studies to identify the cell and molecular biological and other basis for these differences and be able to utilize this information for stratification in order to improve outcome for both women and men.

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Keywords : gender differences, micro-fragmented adipose tissue, knee osteoarthritis, stem cells

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