

# A Single Intra-Articular Injection of Autologous Micro-Fragmented Adipose Tissue and Chondral Shaving Diminishes Knee Pain and Improves Quality of Life in Patients with Early Osteoarthritis

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**INTRODUCTION:** Due to the continued rise in the mean age of the active population, the social impact of degenerative diseases such as articular cartilage pathology is steadily increasing. Articular cartilage lesions are generally associated with symptoms, such as joint pain and reduced function, and with disability, and often progress to end-stage osteoarthritis (OA). A variety of non-invasive and non-surgical strategies have been implemented with variable success rates. Joint-preserving surgical treatments provide temporary relief from symptoms, but the clinical findings are not consistent and many physicians contraindicate their use for diffuse joint degeneration. Thus, new therapeutic approaches, such as the use of mesenchymal stem cells have been developed. The use of adipose-derived stem cells (ASCs) has created substantial interest in the context of cartilage regeneration and their use has produced promising clinical outcomes. However, published studies to date have used complex multi-step processes, which are expensive and involve the use of scaffolds, cells, and growth factors, either alone or in combination with each other. The availability of minimally manipulated adipose tissue that provides, in one-step, the key elements to support a natural regenerative response would have remarkable clinical relevance. The aim of this retrospective study was to explore whether a commercially available technique, the Lipogems<sup>®</sup> system, that intra-operatively provides micro-fragmented and minimally manipulated adipose tissue (referred to as Lipogems), together with a chondral shaving procedure, could improve symptoms and function in patients affected by early knee OA.

**METHODS:** Thirty-five patients affected by early OA underwent an arthroscopic procedure associated with an injection of autologous and micro-fragmented adipose tissue. The indication for the treatment was knee chondropathy grade > II (ICRS classification), constant pain and failure of conservative treatments (physiotherapy, corticosteroids, HA and/or PRP) for at least 12 months. Contraindications for the treatment was synovitis, OA Kellgren-Lawrence grade >III, axial defects >10°, metabolic disorders and BMI > 40. Pre-operative assessments included standard X-rays, MRI, direct physical examination, Knee Injury and Osteoarthritis Outcome Score (KOOS) questionnaire. In addition to injection of Lipogems, patients underwent a chondral shaving procedure (group SH, n=21) or meniscectomy, for those with a meniscal injury no longer repairable (group SM, n=14). All the procedures were performed by the same operators. The lower or lateral abdomen was chosen as donor site for adipose tissue harvesting. Harvested fat was immediately processed in the Lipogems processing kit. The entire process, carried out in one surgical step, was performed in complete immersion in physiological solution minimizing any trauma to the cells. Micro-fragmented fat (10 cc) was injected intra-articularly after the arthroscopic procedure. Standard clinical evaluations at 1, 3, 6, and 12 months post-op included KOOS questionnaire and direct physical examination with the evaluation of knee range of motion, patellar subluxation, ability to walk, navigate up and down the stairs, squatting, muscular strength, stiffness and knee swelling. The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) was calculated from the KOOS. For statistical comparisons, the chi-squared test for all categorical data, Student's t-test for unpaired groups for parametric data, and Mann-Whitney test for non-parametric data (calculated with the Kolmogorov-Smirnov normality test) were used (GraphPad Prism v5.0, La Jolla, USA). A p<0.05 was considered statistically significant. The study was approved by the Regional Ethics Committee of Liguria - Italy (protocol 164REG2016, September 22, 2016). All the procedures mentioned in this study were carried out in accordance with ethical standards and with the Helsinki Declaration of 1975, as revised in 2000. Patients were informed about risks, benefits, and alternative options to the proposed treatment and signed the informed consent form.

**RESULTS SECTION:** Analysis of patients receiving Lipogems and chondral shaving (group SH) revealed a steady and statistically significant improvement of all clinical scores from pre-operative evaluation to 1, 3, 6, and 12 months follow-up. At 12 months, the average improvement in KOOS compared to pre-operative condition was 29 points in symptoms (p<0.0001), 36 in pain (p<0.0001), 37 in function in daily living (p<0.0001), 51 in sport (p<0.0001) and 54 in the quality of life (p<0.0001; Figure A). Statistically significant differences (p<0.0001) between pre-treatment and follow-up values were found also for the total WOMAC scores. Analysis of patients receiving Lipogems, chondral shaving and meniscectomy (group SM) revealed a steady and statistically significant improvement of all the clinical scores until the 6 month follow-up followed by a slight, but not statistically significant, decrease at 12 months. At 12 months, the average improvement in KOOS compared to pre-operative condition was 17 point in symptoms (p=0.014), 12 in pain (p=0.183), 16 in function in daily living (p=0.027), 24 in sport (p=0.014) and 26 in the quality of life (p=0.002; Figure B). The same trend was found between pre-treatment and follow-up values for the total WOMAC scores (p<0.0001). On average, 92% of SH patients and 74% of SM patients clinically improved and 100% of them were satisfied with the treatment. No adverse events or relevant complications were recorded.

**DISCUSSION:** Techniques for harvesting and processing adipose tissue have evolved rapidly in recent years, and published data has demonstrated both the safety and efficacy of using fat and its derivatives for cartilage repair. The current study used a novel one-step method for the lipoaspiration, processing and deployment of adipose tissue (the Lipogems kit). The results demonstrated that, when associated with a shaving procedure, autologous micro-fragmented adipose tissue can improve knee pain and function at least until 1-year follow-up, with a trend of steady increase during this time. Indeed, a constant and statistically significant improvement of all clinical scores was observed from pre-operative evaluation to the 1, 3, 6, and 12 months follow-up, with KOOS sport and quality of life being the most improved scores. An important finding of this study, in addition to the constant improvement of all the clinical scores from baseline evaluation to the 1, 3, 6, and 12 months follow-up, was that no patient worsened compared to the pre-operative condition or underwent additional treatments. Of note, patients very active in sport still improved, demonstrating that patients with high functional demands benefit from this treatment.

**SIGNIFICANCE/CLINICAL RELEVANCE:** The results of this study show the safety and efficacy of using autologous micro-fragmented and minimally manipulated adipose tissue injection associated with arthroscopic chondral shaving for the treatment of diffuse knee chondropathy. The single-step procedure is easy, fast, minimally invasive, safe, and provides a sustainable clinical benefit.

