Attached are a selection of articles supporting the use of adipose-derived stromal cells (mesenchymal stem cells) for the treatment of both osteoarthritis and wounds. There are many studies in the literature using multiple different stem cell sources.

Themes from the articles include clinical and radiographic improvement with therapy, adipose-derived MSC superiority over bone marrow-derived MSC, the utilization of fresh MSCs without culture expansion, and the lack of any need for enzymatic digestion (such as collagenase) for tissue harvesting.

Article 1: Koh et al. *Knee Surg Sports Traumatol Arthrosc*. Epub Dec 2013.

Researchers used stromal cells harvested by centrifugation of 100ml of adipose tissue to treat knee osteoarthritis in patients over 65. The stem cells were combined with platelet rich plasma. Patients in this case series received benefits both in terms of clinical symptoms and cartilage healing (or at least stability of cartilage defects) after 2 years.

There were several important findings:

1- Large numbers of stem cells were harvested from a small amount of adipose tissue. Cell culture methods were not required;

2- Characterization of the cells demonstrated mesenchymal stem cell parameters; and

3- Patients had subjective and objective improvement, even though they were over 65 years of age.

Article 2: Kim et al. *Am J Sports Med.* 2014; 42:2424-2434.

In this study researchers used adipose-derived stem cells obtained from centrifugation of 120ml of lipoaspirate to treat ankle cartilage lesions in combination with the standard technique of drilling the bone in the area (so called marrow stimulation). In this controlled study patients who received stem cells had improved subjective and objective outcomes as compared to those who received conventional treatment only.

There were several important findings:

1- This worked in older patients in a disease of refractory cartilage injury;

2- No cell culture or expansion was required to obtain adequate numbers of stem cells; and

3- This was a controlled study as opposed to a case series. Most studies to date have been case series.

Article 3: Conde-Green et al. J Plast Reconstr Aesth Surg. 2010; 63:1375-1381.

This was a study comparing lipoaspirate processing methods from the standpoint of fat grafting. Adipocytes were healthier when gravity separation was performed but mesenchymal stem cells were best concentrated by centrifugation. Collagenase was not used.

There were two important findings:

1- Centrifugation of lipoaspirate is adequate to obtain a pellet rich in mesenchymal stem cells; and

2- Enzymatic digestion is not required.

Fares MY et al. Acta Orthop Belg. 2024 Jun;90(2):319-333.

This is a generally positive review article of 43 studies of mesenchymal stem cell use for osteoarthritis. Included are those showing clinical benefit and others demonstrating radiographic improvement.

Soufan S et al. World J Orthop. 2024 Aug 18;15(8):704-712.

This is a broad review of MSCs as well as other modalities. Of interest is that adipose-derived MSCs appear superior to bone marrow-derived MSCs.

Holzbauer M et al. Cells. 2024 Apr 25;13(9):750.

This is another literature review concluding that evidence exists for both clinical and radiographic improvements in knee osteoarthritis with the use of autologous MSCs.

Xie RH et al. J Orthop Res. 2024 Apr;42(4):753-768.

This is another literature review supporting the superiority of adipose-derived MSCs over those from bone marrow harvest.

Epanomeritakis IE and Khan WS. World J Stem Cells. 2024 Apr 26;16(4):324-333.

This study investigates both the use of nonexpanded adipose-derived MSCs and the need for enzymatic digestion for harvest. The authors conclude that avoiding enzymatic digestion is preferred. In addition, fresh/non-expanded adipose-derived MSCs are optimal as compared to those expanded ex vivo.