

We use cookies to enhance your experience on our website. By clicking 'continue' or by continuing to use our website, you are agreeing to our use of cookies. You can change your cookie settings at any time.

[Continue](#)
[Find out more](#)



OXFORD
ACADEMIC



Mesenchymal stem cell therapy in the treatment of hip osteoarthritis

Rodrigo Mardones, Claudio M. Jofré, L. Tobar, José J. Minguell 

Journal of Hip Preservation Surgery, Volume 4, Issue 2, 1 July 2017, Pages 159–163,

<https://doi.org/10.1093/jhps/hnx011>

Published: 19 March 2017 **Article history** ▼

Abstract

This study was performed to investigate the safety and efficacy of the intra-articular infusion of *ex vivo* expanded autologous bone marrow-derived mesenchymal stem cells (BM-MSK) to a cohort of patients with articular cartilage defects in the hip. The above rationale is sustained by the notion that MSCs express a chondrocyte differential potential and produce extracellular matrix molecules as well as regulatory signals, that may well contribute to cure the function of the damaged hip joint. A cohort of 10 patients with functional and radiological evidences of hip osteoarthritis, either in one or both legs, was included in the study. BM-MSK (the cell product) were prepared and infused into the damaged articulation(s) of each patient (60×10^6 cells in 3 weekly/doses). Before and after completion of the cell infusion scheme, patients were evaluated (hip scores for pain, stiffness, physical function, range of motion), to assess whether the infusion of the respective cell product was beneficial. The intra-articular injection of three consecutive weekly doses of *ex vivo* expanded autologous BM-MSK to

Article Navigation

the statistical significance of the above data is in line with the observation that the radiographic scores (Tönnis Classification of Osteoarthritis) of the damaged leg(s) remained without variation in 9 out of 10 patients, after the administration of the cell product.

Topic: [diagnostic radiologic examination](#), [extracellular matrix](#), [articular cartilage](#), [chondrocytes](#), [hip joint](#), [intra-articular injections](#), [osteoarthritis](#), [hip osteoarthritis](#), [pain](#), [range of motion](#), [safety](#), [leg](#), [stem cell](#), [mesenchymal](#), [infusion procedures](#), [physical function](#), [molecule](#), [treatment effectiveness](#)

Issue Section: [research articles](#)

INTRODUCTION

Osteoarthritis (OA) embodies a recurrent and incapacitating arthritic condition, characterized by the occurrence of damaging joint changes, including cartilage destruction by cytokines, matrix metalloproteinases and prostaglandins. As a consequence, a cascade of deleterious events starts, including subchondral bone remodeling and resorption, hypertrophic differentiation of chondrocytes, neovascularization of synovial tissue and focal joint cartilage calcification. Management of OA has been diverse and included pharmacological therapy treatment options, surgical interventions and orthopedic procedures including total joint replacement and/or joint fusion [1, 2].

Recent advances in regenerative medicine, particularly the optimization of procedures associated with the utilization of stem and progenitor cells, has opened new therapeutic perspectives for the treatment of OA. Given that articular cartilage exhibits little or no ability for self-repair, the option to delivery into the OA injured site a source of progenitor cells capable to differentiate into chondrocytes, appears to be an attractive therapeutic option [3–6].

Mesenchymal stem cells (MSCs) fulfill the above requirements. In addition to differentiate into chondrocytes (which in turn produce and maintain a cartilaginous matrix), MSC produce and secrete a vast array of mediators of cell function, like growth factor and cytokines. And last but not least, the minute number of ‘native’ MSC present in several adult tissues, including the bone marrow, can be easily increased by *ex vivo* procedures [7].

[Skip to main content](#)

[Article Navigation](#)

the function of a damaged joint.

MATERIALS AND METHODS

Patient population

The study was performed at Clinica Las Condes, Santiago, Chile. Clinica Las Condes is affiliated to Johns Hopkins Medicine International and accredited by the Joint Commission International (USA). Procedures carried out in this study were in compliance with regulations established by the Research and Ethics Committees of Clinica Las Condes.

A total of 10 patients with osteoarthritis in one or both hips were enrolled in the study. Main inclusion criteria included age ≥ 60 years, radiological evidence of osteo-degenerative disease changes (level to moderate) in one or both joint hip (s) and pain levels (refractory to analgesics and/or hyaluronic acid or cortisone injection treatment) ≥ 40 (Visual Analog Scale of 100 mm).

Main exclusion criteria included evidence of intra-articular space ≤ 1 mm, indication of cartilage's loss of volume, as measured by magnetic resonance imaging and/or failure to complete the protocol's established number of cell infusions. Clinical characteristics of the study population are given in [Table I](#).

Table I.

Clinical characteristics of the study population at inclusion

Patient characteristics (initials/sex/age)	Comorbidities	Concomitant drug(s) intake	Hip damage location
RPB/f/57	hypothyroidism, arrhythmia, arterial hypertension	Atenolol, Zopiclone Levothyroxine	right
MMP/f/54	hypothyroidism, cervical dysplasia	Syndol, Tramadol	right
DCF/m/60	none	none	right
Skip to Main Content ALH/m/50	dyslipidemia, hypothyroidism	Levothyroxine	right

Article Navigation

MOP/f/54	hypothyroidism, asthma, arterial hypertension	Levothyroxine, Losartan, Budesonide	right
PVV/f/51	none	none	right
FVS/m/24	none	none	left
KOV/f/59	asthma, arterial hypertension, dyslipidemia	Atenolol, Desloratadine	right and left
JPD/m/49	mood disorder	Sertraline	right and left
SPS/m/39	none	Sibutramine	right and left

Study end points

Primary endpoint included the feasibility to prepare from each patient a viable population of 60×10^6 *ex vivo* expanded bone marrow-derived (BM)-MSC. Secondary endpoints included clinical evidence(s) confirming that the infusion of the cell product into the damaged hip(s) was safe and proficient to generate a slowdown in the progression of osteoarthritis.

Preparation of *ex vivo* expanded autologous BM-MSC

For preparation of BM-MSC, all patients underwent bone marrow aspiration (30 ml) from the posterior iliac crest. In the case of patients receiving BM-MSC infusion on both legs, the volume of bone marrow aspiration was 60 ml. Bone marrow aspirates were sent to the GMP facility for isolation and *ex vivo* expansion of bone marrow-resident MSC.

Shortly, the *ex vivo* expansion procedures included, (i) processing of bone marrow aspirates by density separation to isolate a fraction of mononuclear cells (BM-MNC), and b) the expansion, by means of cell culture procedures, of the minor population of 'native' MSC present in BM-MNC [7, 8]. At the end of the expansion procedures, the resulting population of autologous BM-MSC (the cell product) was assessed for cell number, viability, microbiological condition and expression of distinctive MSC cell membrane markers [9]. In addition, flow cytometry analysis proved that the *ex vivo* manipulations did not triggered changes in MSC's attributes [10].

[Skip to Main Content](#)

Cell infusion

[Article Navigation](#)

Subsequently, the damaged hip (s) of each patient received the infusion of 20×10^6 *ex vivo* expanded BM-MSC. After 7 and 14 consecutive days, patients received the infusion of a second and a third dose of the respective cell product [4, 11]. Thus, within a period of 14 days, the damaged hip(s) of each patient received the infusion of 60×10^6 *ex vivo* expanded autologous MSC.

Clinical outcome assessment

Clinical data were prospectively collected during the study period (May 2013 to September 2016) and included evaluation of pain, stiffness, physical function and range of motion. For this, the following specific scores were used: Harris Hip (HHS), Visual Analog (VAS), Vail Hip and Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC). Additionally, Tonnis X-ray measurements of the hip joint(s) were performed to evaluate changes in the progression of osteoarthritis [5, 11, 12].

RESULTS

Preparation and infusion of *ex vivo* expanded bone marrow-derived autologous MSC

After bone marrow aspiration, no bleeding, infection and/or other complications were identified. In turn, *ex vivo* expanded autologous BM-MSCs manufactured for all patients, fulfilled the established rigorous release criteria for infusion [9, 10]. Accordingly, the infusion of the autologous cell product (three doses per damaged hip) was well tolerated and no complications and/or adverse events occurred post-infusion.

Clinical outcome

To assess whether the infusion of the cell product was beneficial patients were tested before and at different times after completing the cell infusion schedule. As shown in [Table II](#), raw data analysis using a cartilage injury evaluation package, indicated that in all patients the infusion of the cell product bring about an improvement in pain, function and range of motion during the follow-up period of 16–40 months after cell infusion. The statistical significance of the above data is shown in [Table III](#). In line with this observation, the

[Skip to Main Content](#)

[Article Navigation](#)

product ([Table II](#)).

Table II.

Clinical outcomes after MSC infusion by using a cartilage injury evaluation package including pain, function, range of motion and radiographic evaluation

Patient ^a	Leg treated ^b	VASC ^c		WOMAC ^d		HHSM ^e		VAIL ^f		Tonnis ^g		Last follow up (month after infusi
		Pre	post	Pre	post	Pre	post	Pre	post	Pre	post	
KOV	L	3	0	21	4	66	98	55	88	I	I	16
	R	2	0	10	4	10	78	86	78	I	I	16
SPS	L	4	2	13	13	69	71	55	55	II	I	22
	R	1	1	3	0	95	100	92	100	II	II	22
RPB	R	5	2	70	51	72	83	47	55	II	II	24
ALH	L	6	1	89	74	72	96	55	86	II	II	27
MMP	R	8	2	51	30	40	75	45	68	II	II	28
PVV	L	4	2	40	32	63	62	34	42	III	III	29
FVS	L	4	0	12	10	68	100	69	99	II	II	29
MOP	R	5	3	82	14	36	72	56	76	II	II	30
DCF	R	6	1	34	13	62	83	69	82	II	II	34
JPD	L	2	0	8	0	82	100	73	100	II	II	40
	R	4	0	16		70	96	59	88	III	III	40

^a initials;

^b L, left; R, right;

^c pain scale;

Article Navigation

- hip function;
- ^f hip function;
- ^g radiographic evaluation.

Table III.

Statistical significance of the clinical effects elicited by the infusion of *ex vivo* expanded autologous BM-MSc into patients with hip osteoarthritis

Hip scores	Pre-infusion values (mean ± SEM)	Post-infusion values (mean ± SEM)	P-value
VAS	4.2 ± 0.5	1.1 ± 0.3	0.0001
WOMAC	34.5 ± 8.2	19.2 ± 6.1	0.15
HHSM	61.9 ± 6.1	85.7 ± 3.9	0.003
VAIL	61.2 ± 4.5	78.2 ± 5.2	0.02

DISCUSSION

Several techniques, including micro fracture, autologous chondrocyte implantation, and mosaicplasty have been used for the treatment of symptomatic chondral lesions in the hip. Nevertheless, to date there is still no definitive solution to reproducibly replicate the load-bearing capacity and durability of native joint cartilage [1, 2, 4]. Consequently, new therapeutic options based in the use of MSC have been initiated.

Even though strong evidences indicate that clinical use of MSC is feasible and safe [4, 5], confirmation for their clinical efficacy still remain controversial [13–15].

The results presented in this clinical study, revealed that shortly after the intra articular infusion of a cell product consisting of *ex vivo* expanded autologous BM-MSc, an improvement in hip function occurred. The reparative effect, which is fully maintained over time (Table II), proved to be free of major complications or side effects during the prolonged follow-up period. Moreover, the radiographic scores of the hip joint(s), assessed on a time period ranging from 7 to 30 months after cell infusion, clearly demonstrate a halt in the progression of osteoarthritis.

[Skip to Main Content](#)

Article Navigation

employed in this study, privileged quality than quantity of cell product to be administered to the patient [9, 10], and (ii) based in previous observations, the cell product was administered to the patient, instead of 1 in 3 consecutive weekly doses [4–11]. Further studies will contribute to validate and confirm the above statements.

ACKNOWLEDGEMENTS

We would like to acknowledge the dedicated contribution of clinicians researchers, and nurses at the Centro de Terapia Regenerativa Celular and Centro de Traumatología y Ortopedia, Clínica Las Condes, Santiago, Chile.

CONFLICT OF INTEREST STATEMENT

None declared.

REFERENCES

- 1 Pulsatelli L, Addimanda O, Brusi V et al. New findings in osteoarthritis pathogenesis: therapeutic implications. *Ther Adv Chronic Dis* 2013; 4: 23–43.
[Google Scholar](#) [Crossref](#) [PubMed](#)
- 2 Thysen S, Luyten FP, Lories RJ. Targets, models and challenges in osteoarthritis research. *Dis Model Mech* 2015; 8: 17–30.
[Google Scholar](#) [Crossref](#) [PubMed](#)
- 3 Diekman BO, Guilak F. Stem cell-based therapies for osteoarthritis: Challenges and opportunities. *Curr Opin Rheumatol* 2013; 25: 119–26.
[Google Scholar](#) [Crossref](#) [PubMed](#)
- 4 Mardones R, Larrain C. Cartilage restoration technique of the hip. *J Hip Preservation Surgery* 2015; 3: 30–6.
[Skip to Main Content](#) [Google Scholar](#) [Crossref](#)
- 5 Jo CH, Lee YG, Shin WH et al. Intra-articular injection of mesenchymal stem cells for the

[Article Navigation](#)

[Google Scholar](#) [Crossref](#) [PubMed](#)

- 6 Mardones R, Jofré CM, Minguell JJ. Cell Therapy and Tissue Engineering Approaches for Cartilage Repair and/or Regeneration. *Int J Stem Cells* 2015; 8: 48–53.

[Google Scholar](#) [Crossref](#) [PubMed](#)

- 7 Minguell JJ, Allers C, Lasala GP. Mesenchymal stem cells and the treatment of conditions and diseases: the less glittering side of a conspicuous stem cell for basic research. *Stem Cells Dev* 2013; 22: 193–203.

[Google Scholar](#) [Crossref](#) [PubMed](#)

- 8 Lasala GP, Minguell JJ. Bone marrow-derived stem/progenitor cells: their use in clinical studies for the treatment of myocardial infarction. *Heart Lung Circ* 2009; 18: 171–80.

[Google Scholar](#) [Crossref](#) [PubMed](#)

- 9 Dominici M, Le Blanc K, Mueller I et al. Minimal criteria for defining multipotent mesenchymal stromal cells. The International Society for Cellular Therapy position statement. *Cytotherapy* 2006; 8: 315–7.

[Google Scholar](#) [Crossref](#) [PubMed](#)

- 10 Madeira A, da Silva CL, dos Santos F et al. Human mesenchymal stem cell expression program upon extended *ex-vivo* cultivation, as revealed by 2-DE-based quantitative proteomics. *Plos One* 2012; 7:e43523.

[Google Scholar](#) [Crossref](#) [PubMed](#)

- 11 Mardones R, Tovar L, Tomic A, Diaz C, Salineros M, Guendelman E. Use of expanded autologous msc (mesenchymal stem cells) injections after complex cartilage FAI hip scope procedure. *12th World Congress of International Cartilage Repair Society* . Chicago, USA, 2015.

- 12 Brokelman RB, Haverkamp D, van Loon C, Hol A, van Kampen A, Veth R. The validation of the visual analogue scale for patient satisfaction after total hip arthroplasty. *Eur Orthop Traumatol* 2012; 3: 101–10.

[Google Scholar](#) [Crossref](#) [PubMed](#)

[Skip to Main Content](#)

- 13 Jordan MA, Van Thiel GS, Chahal J, Nho SJ. Operative treatment of chondral defects in the hip joint: a systematic review. *Curr Rev Musculoskelet Med* 2012; 5: 244–53.

[Article Navigation](#)

14 Koh YG, Jo SB, Kwon OR et al. Mesenchymal stem cell injections improve symptoms of knee osteoarthritis. *Arthroscopy* 2013; 29: 748–55.

[Google Scholar](#) [Crossref](#) [PubMed](#)

15 Filardo G, Perdisa FA, Marcacci M, Kon E. Stem cells in articular cartilage regeneration. *J Orthop Surg Res* 2016; 11: 42.

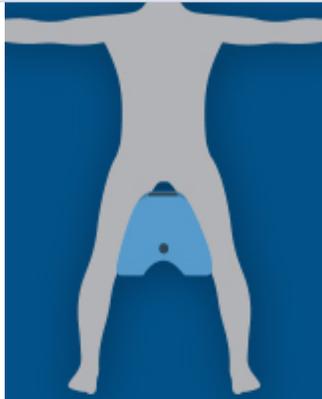
[Google Scholar](#) [Crossref](#) [PubMed](#)

© The Author 2017. Published by Oxford University Press

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/4.0/>), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited. For commercial re-use, please contact journals.permissions@oup.com

[Skip to Main Content](#)

Article Navigation



Flex PPU

-  Avoid Perineum Pressure
-  Lock and Align Patient
-  Redirect Traction Force

[Click for a free sample](#)

 **ARTHRAFIT™**

[View Metrics](#)

Email alerts

[New issue alert](#)

[Advance article alerts](#)

[Article activity alert](#)

[Skip to Main Content](#)

Article Navigation

from Oxford Academic

More on this topic

Efficacy of a non-image-guided diagnostic hip injection in patients with clinical and radiographic evidence of intra-articular hip pathology

Previous failed hip arthroscopy negatively impacts early patient-reported outcomes of the periacetabular osteotomy: an ANCHOR Matched Cohort Study

Higher patient activity level and subchondral stiffening in asymptomatic cam femoroacetabular impingement subjects

Medial synovial fold cyst in the hip leading to pectineofoveal impingement

Related articles in PubMed

Remote Ischemic Preconditioning Acutely Improves Coronary Microcirculatory Function.

Porphyrin-Based SOD Mimic MnTnBu OE -2-PyP⁵⁺ Inhibits Mechanisms of Aortic Valve Remodeling in Human and Murine Models of Aortic Valve Sclerosis.

The Cellular Biology of Fracture Healing.

Comparative effects of proximal and distal small intestinal administration of metformin on plasma glucose and glucagon-like peptide-1, and gastric emptying after oral glucose, in type 2 diabetes.

[Skip to Main Content](#)

Citing articles via

[Article Navigation](#)[Google Scholar](#)[CrossRef](#)**Latest** | **Most Read** | **Most Cited**

Simultaneous pigmented villonodular synovitis and synovial chondromatosis of the hip: case report

Impact, impact, impact What the papers say

Quadratus lumborum block provides improved immediate postoperative analgesia and decreased opioid use compared with a multimodal pain regimen following hip arthroscopy

The education and training of future hip preservation surgeons: aggregate recommendations of high-volume surgeons

[Skip to Main Content](#)

Article Nav



[About Journal of Hip Preservation Surgery](#)

[Editorial Board](#)

[Policies](#)

[Author Guidelines](#)

[Facebook](#)

[Twitter](#)

[YouTube](#)

[Advertising and Corporate Services](#)

[Journals Career Network](#)



**INTERNATIONAL SOCIETY
FOR HIP ARTHROSCOPY**

Online ISSN 2054-8397

Copyright © 2018 Oxford University Press

[About Us](#)

[Contact Us](#)

[Careers](#)

[Help](#)

[Access & Purchase](#)

[Rights & Permissions](#)

[Open Access](#)

Resources

[Authors](#)

[Librarians](#)

[Societies](#)

Connect

[Join Our Mailing List](#)

[OUPblog](#)

[Twitter](#)

[Facebook](#)

[YouTube](#)

[Tumblr](#)

Explore

[Shop OUP Academic](#)

[Oxford Dictionaries](#)

[Oxford Index](#)

Sponsors & Advertisers

Epigeum

Press & Media

OUP Worldwide

Agents

University of Oxford

Oxford University Press is a department of the University of Oxford. It furthers the University's objective of excellence in research, scholarship, and education by publishing worldwide

OXFORD
UNIVERSITY PRESS

Copyright © 2018 Oxford University Press

[Cookie Policy](#)

[Privacy Policy](#)

[Legal Notice](#)

[Site Map](#)

[Accessibility](#)

[Get Adobe Reader](#)