Analysis of the RACS scholarship programme over the last 5 years (2012–2016) demonstrates a total number of 405 applicants, with 166 scholarships/Fellowships awarded. This gives a success rate of 41%, which is not only encouraging, being higher than that of the National Health and Medical Research Council[3] (at approximately 20% for Career Development Fellowships and 16% for Project Grants), but also reflects the competitive nature of the RACS scholarship programme. Furthermore, the level of funding per-capita for RACS is approximately $1.8 million per annum for 6086 Fellows and 1245 Trainees,[4] which encouragingly is similar to that of the Royal College of Surgeons of England which awards the equivalent of approximately $5 million for 20 000 members (equating to a similar level of funding per person in each college).

An important outcome to note from this review is that 78% of respondents were able to achieve a higher degree as a result of the scholarship programme despite the majority of the scholarships having a 1-year term. This would imply that it might be beneficial to increase the duration of a number of the scholarships to a 2- or 3-year term. Without further donations, however, this may be difficult to establish and sustain.

Other direct outcomes from the scholarship and the impact on scholars' careers and quality of health care are difficult to objectively analyse. However, it was encouraging to note that 90.0% of scholars believed they had acquired the skill of critically evaluating scientific information and 67.5% of respondents significantly improved their non-technical skills which are important attributes for all surgeons to accrue, and 70.7% of scholars conducted further independent research following the scholarship-funded period. Furthermore, almost half of the scholars received subsequent research grants that were not awarded by the RACS.

The RACS scholarship programme has succeeded in supporting Surgical Trainees/Junior Fellows and makes key contributions to the surgery-related scientific literature.

References

1. Hebert RS, Levine RB, Smith CG, Wright SM. A systematic review of resident research curricula. *Acad. Med.* 2003; **78**: 61–8.
2. Millis SR, Campagnolo DI, Kirshblum S, Elovic E, Jain SS, DeLisa JA. Improving resident research in physical medicine and rehabilitation: impact of a structured training program. *J. Spinal Cord Med.* 2004; **27**: 428–33.
3. McCallum J. *NHMRC - What are Australia's Core Competencies and Competitive Advantages in Medical Research*? Edition. [Cited 27 Jan 2016.] Available from URL: http://www.slideshare.net/informaoz/0900-professor-john-mccallum
4. Royal College of Surgeons of England. *Activities Report*. Edition. [Cited 27 Jan 2016.] Available from URL: https://www.surgeons.org/media/21713909/activities-report-jan-dec-2014.pdf

Tamsin J. Garrod,* PhD
Wendy J. Babidge,* PhD
Susan Pleass,*
Ian C. Bennett,† FRACS
David F. Scott,† AM, FRACS
*Research, Audit and Academic Surgery, Royal Australasian College of Surgeons, Adelaide, South Australia, Australia and †Royal Australasian College of Surgeons, Melbourne, Victoria, Australia

doi: 10.1111/ans.13763

Stem cells and knee osteoarthritis: a legitimate treatment option?

Osteoarthritis (OA) is a degenerative disease that causes pain, stiffness and decreased function. Treatment utilizing mesenchymal stem cells (MSCs) has become a focus of interest as the successful regeneration of cartilage represents a new minimally invasive, non-surgical alternative. Yet, is it a truly legitimate treatment option?

Presently, there are various treatment measures, including microfracture and subchondral drilling, which are performed in an attempt to regenerate articular cartilage. These modalities are generally reserved for defects less than 2–3 cm^2 and in patients younger than 40 years.[1] As such, this review addresses only the potential for treatment of advanced OA as well as the lack of quality evidence.

MSCs are pluripotent adult stem cells found in numerous human tissues, including bone marrow and adipose tissue. These MSCs are then placed into various growth factors to mature into higher numbers. The product is then injected into the damaged joint or bound with a scaffold and imbedded into an area of defect. A signal is then introduced to begin the cell differentiation process into articular cartilage[2] (Fig. 1).

Bone marrow-derived MSCs have been utilized in patients who were unresponsive to conservative therapy. Patients reported subjective improvement in symptoms, whilst objective results are limited to apparent improvements in clinical examination.[4]

Arthroscopic surgery has been used to objectively classify cartilage defects using the International Cartilage Repair Society (ICRS) grading system. Koh *et al.* treated 37 patients with adipose-derived MSCs, and at mean follow-up of 26.5 months, 76% of cartilage lesions remained in the abnormal or severely abnormal state. Authors concluded that tissue-engineered scaffolds may be needed to improve cartilage repair.[5]

Tissue-engineered scaffolds, such as fibrin glue, have been postulated to improve osteochondral regeneration.[6] However, there is no evidence to date that shows a statistically significant difference between treatment and control groups.[7] In addition, using a higher dose of MSCs has shown improvement in osteochondral regeneration,[8] yet it cannot be concluded that a higher dose is more effective than an optimal patient dose, which is currently unknown.

Encouraging results have been reported with combination therapy using adipose-derived MSCs with platelet-rich-plasma and arthroscopic lavage. However, it is impossible to determine whether

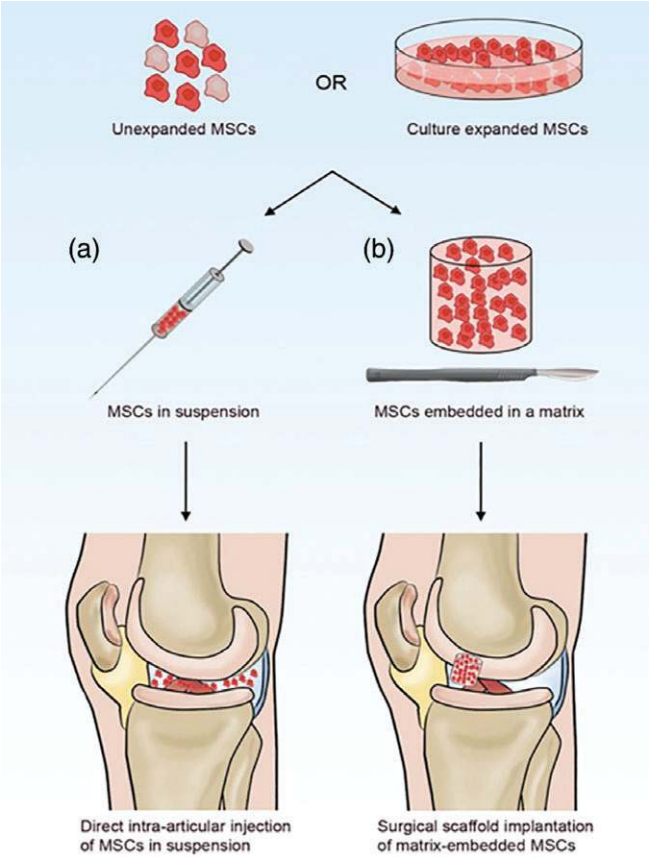

Fig. 1. Alternate means of delivery of MSCs into cartilage lesions in knee OA. (a) Direction intra-articular injection of MSCs in solution. (b) Direct surgical implantation of MSCs in matrix scaffold. Reproduced from Kristjánsson and Honsawek,[3] with permission.

the improvements are because of the MSCs alone. Furthermore, it is indeterminate regarding which dose of MSCs are most effective as the amount of cells injected varied considerably between patients.[9]

There is a high number of *in vivo* animal works currently underway to scientifically demonstrate the efficacy of MSC therapy. Furthermore, there are a number of human trials proceeding, including three trials in Australia that are either in the recruiting phase or not yet started.

It would seem that the implantation of MSCs might be a viable and effective treatment alternative for patients' suffering from knee OA. Despite the favourable evidence, one must look at the quality of the studies. Published literature to date only includes individual case reports or a small cohort sample. The outcome measures used are mostly subjective, making it difficult to determine whether any improvement is simply because of a placebo effect. In addition, examination performed by the relevant authors evokes the potential for variability and bias. Most notably, there are no published clinical data on the long-term outcomes and complications of this treatment, and the ideal dose of therapy remains unknown.

Clinics in Australia offering MSC therapy raise hope about the treatability of advanced knee OA, although its safety and efficacy has not been established. As a result, the National Health and Medical Research Council do not recommend the use of MSCs for the treatment of knee OA.

Internationally, stem cell clinics can be located in countries with variable standards of medical care. The significant financial burden of travel expenses combined with an unproven treatment can cause patient harm, even if they do not directly cause adverse health effects.

Whilst it is ultimately the patient's decision whether they decide to undertake unproven MSC treatment or not, medical practitioners have a responsibility to ensure their patient makes a well-informed decision and understands the potential risks. Therefore, clinicians need to remain aware of the lack of robust evidence and use MSCs at their own discretion.

References

1. Madry H, Grün UW, Knutsen G. Cartilage repair and joint preservation: medical and surgical treatment options. *Dtsch. Arztebl. Int.* 2011; **108**: 669–77.
2. Centeno CJ, Busse D, Kisiday J, Keohan C, Freeman MM. Increased knee cartilage volume in degenerative joint disease using percutaneously implanted, autologous mesenchymal stem cells, platelet lysate and dexamethasone. *Ann. Transplant.* 2008; **9**: 246–51.
3. Kristjánsson B, Honsawek S. Current trends of stem cell-based approaches for knee osteoarthritis. *OA Tissue Eng.* 2013; **1**: 7.
4. Orozco L, Munar A, Soler R *et al.* Treatment of knee osteoarthritis with autologous mesenchymal stem cells: a pilot study. *Transplantation* 2013; **95**: 1535–41.
5. Koh YG, Choi YJ, Kwon OR, Kim YS. Second-look arthroscopic evaluation of cartilage lesions after mesenchymal stem cell implantation in osteoarthritic knees. *Am. J. Sports Med.* 2014; **42**: 1628–37.
6. Pak J. Regeneration of human bones in hip osteonecrosis and human cartilage in knee osteoarthritis with autologous adipose-tissue-derived stem cells: a case series. *J. Med. Case Rep.* 2011; **5**: 296.
7. Kim YS, Choi YJ, Suh DS *et al.* Mesenchymal stem cell implantation in osteoarthritic knees: is fibrin glue effective as a scaffold? *Am. J. Sports Med.* 2014; **27**: 1–10.
8. Jo CH, Lee YG, Shin WH *et al.* Intra-articular injection of mesenchymal stem cells for the treatment of osteoarthritis of the knee: a proof-of-concept clinical trial. *Stem Cells* 2014; **32**: 1254–66.
9. Koh YG, Choi YJ, Kwon SK, Kim YS, Yeo JE. Clinical results and second-look arthroscopic findings after treatment with adipose-derived stem cells for knee osteoarthritis. *Knee Surg. Sports Traumatol. Arthrosc.* 2015; **23**: 1308–16.

James Wheeler,* MBBS, BPhty
Danè Dabirrahmani,† MBiomedE, BE (Mech) (Hons)
Nigel Hope,* MBBS, PhD, FRACS, FAOrthA
**School of Medicine, The University of Notre Dame Australia, Darlinghurst, New South Wales, Australia and †Faculty of Medicine and Health Sciences, Macquarie University, Sydney, New South Wales, Australia*

doi: 10.1111/ans.13640