

# Future Trends for Unicompartmental Arthritis of the Knee: Injectables & Stem Cells

Marco Kawamura Demange, MD, PhD<sup>a,b</sup>, Marco Sisto, BA<sup>b</sup>,  
Scott Rodeo, MD<sup>b,\*</sup>

## KEYWORDS

- Arthritis • Knee arthritis • Injectable arthritis treatment • Osteoarthritis
- Hyaluronic acid • Stem cell

## KEY POINTS

- Intra-articular corticosteroids and hyaluronic acid injections have a role in the treatment of early arthritis of the knee.
- Platelet-rich plasma (PRP) injections alone do not promote cartilage repair.
- The role of PRP injections in early knee osteoarthritis and focal cartilage lesions still needs to be better understood.
- Ultimately, combinations of various injectable materials may be useful in treating early knee osteoarthritis.
- Stem cell therapy has potential as either an isolated approach or combined with different surgical procedures.
- Gene therapy is a possibility but probably will not be available in the near future.

## INTRODUCTION

Arthritis is one of the most frequent musculoskeletal problems, causing pain, disability, and a significant economic burden. In terms of prevalence, as life expectancy increases, arthritis prevalence will also increase.<sup>1,2</sup> There are estimates that osteoarthritis (OA) may become the fourth-highest impact condition in women and the eighth-most important condition in men in the developed world.<sup>3</sup>

There is no consensus about the best treatment option for early knee arthritis. Nonsurgical options include oral medications, injections, orthoses, physiotherapy, and lifestyle modification.<sup>4,5</sup> The main surgical options for arthritis of the knee after failure of a nonsurgical therapy include arthroscopic surgical procedures, cartilage repair

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<sup>a</sup> Department of Orthopedic Surgery and Traumatology, University of São Paulo, Rua Ouvidio Pires de Campos, 333 São Paulo, SP 05403-010, Brazil; <sup>b</sup> Hospital for Special Surgery, Weil Cornell Medical College, 535 E 70th Street, New York, NY 10021, USA

\* Corresponding author.

E-mail address: [rodeos@hss.edu](mailto:rodeos@hss.edu)

or transplantation, realignment osteotomies, unicompartmental arthroplasties, or total knee arthroplasties.<sup>4,5</sup>

One of the main issues concerning early knee OA is that there are currently no treatment options that are able to completely revert the cartilage degenerative process. Ideally, the goal of nonsurgical treatments is to retard or stop the degenerative process. Despite the presence of unicompartmental arthritis, many patients still choose to participate in high-impact activities that can result in joint discomfort and pain. As a result, there has been a large effort to develop injectable treatments that relieve symptoms and delay the progression of early OA.

Cartilage focal lesions are also common in the adult population and may progress to arthritis.<sup>6,7</sup> Various knee disorders, including anterior cruciate ligament (ACL) tears,<sup>8,9</sup> meniscal tears and previous meniscectomies,<sup>7</sup> disruption of the subchondral bone,<sup>10,11</sup> and limb malalignment,<sup>12</sup> may lead to the development of cartilage lesions or progression to arthritis. Early treatment of focal cartilage lesions and early knee arthritis may be a possible approach to prevent progression of knee OA.<sup>6,7,13-15</sup>

In this article, we discuss current nonsurgical injectable treatment options, as well as future trends for cartilage lesions and early arthritis of the knee. We also cover some potential treatments for knee OA, including stem cell and gene therapies.<sup>16,17</sup>

## CURRENT TREATMENT OPTIONS

### *Corticosteroid Injections*

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Corticosteroid injections have been performed in the treatment of knee OA for decades.<sup>18,19</sup> Recent systematic reviews have discussed the efficacy of corticosteroids compared with placebo. Similarly, recent studies have compared corticosteroids with other injectable treatment options, such as platelet-rich plasma (PRP) or hyaluronic acid (HA).<sup>20</sup> Corticosteroid injections may be performed alone, combined with other medications, or after knee arthroscopies.<sup>16,21</sup> The exact mechanism of the therapeutic effect of corticosteroids in knee OA is still unclear; however, it is believed to be related to the anti-inflammatory effect of the drug.<sup>20</sup> The short-term benefits of intra-articular corticosteroid injections are well established. The administration of steroid injections either alone or combined with local anesthetics has been shown to be a viable short-term option and is universally accepted in clinical practice as such.<sup>22</sup> The long-term benefits have not been confirmed and chronic use may lead to progressive cartilage degeneration. Maricar and colleagues<sup>20</sup> recently published a systematic review regarding intra-articular corticosteroid injection and predictors in knee OA. Within 696 publications, only 11 matched their inclusion criteria, but only 2 trials had a primary aim to determine predictors of response to corticosteroids. The investigators could not conclusively identify any predictors of response to intra-articular use of corticosteroids in knee OA, but they reported that synovitis and knee effusion may have some correlation with clinical improvement.<sup>20</sup>

### *Autologous-Conditioned Serum*

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Cytokines play an important role in the mechanism of OA. Interleukin-1 (IL-1) is known as one of the most important catabolic cytokines in the cartilage breakage process. The human body naturally produces an IL-1 receptor antagonist (IL-1ra), which is believed to have the potential to limit the intra-articular effects of the catabolic cytokine IL-1. Autologous-conditioned serum is generated by incubation of venous blood with glass beads.<sup>23,24</sup> After incubation for 24 hours at 37°C, the blood is recovered and centrifuged. Blood monocytes are a major natural source of IL-1ra and their production of IL-1ra is greatly stimulated by culture on immunoglobulin G-coated plates.

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