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Swiss doctors report success of using cells from the nose to repair damaged knee joints

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Writing in *The Lancet*, Swiss doctors report that cartilage cells harvested from patients' own noses have been used to successfully produce cartilage transplants for the treatment of the knees of 10 adults (aged 18-55 years) whose cartilage was damaged by injury. Two years after reconstruction, most recipients reported improvements in pain, knee function, and quality of life, as well as developing repair tissue that is similar in composition to native cartilage.

Despite this promising start, however, the effectiveness of the procedure needs to be rigorously assessed in larger randomised trials compared to conventional treatments and with longer follow up before any firm conclusions can be drawn about its use in routine clinical practice, say the authors.

Every year, around 2 million people across Europe and the USA are diagnosed with damage to articular cartilage because of injuries or accidents. Articular cartilage is the tissue on the end of a bone that cushions the surface of the joint and is vital for painless movement. Because the tissue doesn't have its own blood supply, it has limited capacity to repair itself once damaged, leading to degenerative joint conditions like osteoarthritis. Traditional methods to prevent or delay onset of cartilage degeneration following traumatic events like microfracture surgery don't create the healthy cartilage needed to endure the forces of everyday movement. Even novel medical advances using patients' own articular cartilage cells (chondrocytes) have been unable to predictably restore cartilage structure and function in the long term. As

the population ages and people live longer, there is an urgent and growing need to develop an effective therapy to repair cartilage damage.

A team from the University Hospital Basel in Switzerland investigated an alternative approach using engineered cartilage tissue grown from patients' own cartilage cells from the nasal septum which have a unique capacity to grow and form new cartilage tissue. This phase 1 study included 10 patients with full-thickness cartilage lesions of the knee. The researchers extracted a small biopsy specimen (6mm in diameter) from the nasal septum under local anaesthetic using a minimally invasive procedure. The harvested cells were multiplied by exposing them to growth factors for 2 weeks. The expanded cells were then seeded onto collagen membranes and cultured for 2 additional weeks, generating a 30 x 40mm cartilage graft. The engineered graft was then cut into the right shape and used to replace damaged cartilage that was surgically removed from the recipient's knee (figure 1).

Despite variable degrees of defect filling, MRI scans at 2 years revealed the development of new tissue with similar compositional properties of native cartilage (figure 4). Moreover, nine recipients (one was excluded because of several independent sports injuries) reported substantial improvements in the use of their knee and in the amount of pain compared to before surgery. No adverse reactions were reported, although two serious adverse events unrelated to the procedure were recorded—an independent injury in the opposite knee and new cartilage lesions at other locations in the treated knee (table 2).

The researchers say that the small number of participants and the relatively short follow-up time will mean further studies will be needed. Similar to other early phase surgical studies, the trial did not involve a control group, so other studies will be needed to establish a comparison in effectiveness with currently available treatments, and to assess the possible bias of a placebo effect.

According to lead author Ivan Martin, Professor of tissue engineering at the University of Basel and University Hospital Basel in Switzerland, "Our findings confirm the safety and feasibility of cartilage grafts engineered from nasal cells to repair damaged knee cartilage. But use of this procedure in everyday clinical practice is still a long way off as it requires rigorous assessment of efficacy in larger groups of patients and the development of manufacturing strategies to ensure cost effectiveness. Moreover, in order to extend the potential use of this technique to older people or those with degenerative cartilage pathologies like osteoarthritis, a lot more fundamental and pre-clinical research work needs to be done."

Writing in a linked Comment, Dr Nicole Rotter from Ulm University Medical Center and Dr Rolf Brenner from the University of Ulm, Ulm, in Germany say, "Overall, this first-in-human trial represents an important advance towards less invasive, cell-based repair technologies for articular cartilage defects, because the site of tissue harvest is not located within the healthy part of a joint, avoiding potential side-effects of harvesting. With respect to possible applications in older patients, it could be a promising observation that tissue-engineered cartilage based on nasal chondrocytes did not show substantial dependence on donor age. However, long-term results—including data for integration and histological quality of the repair tissue, placebo-controlled or current treatment-controlled trials, and analysis of cost-effectiveness—will be needed to establish whether this technology has the potential to be approved by the European Medicines Agency and the US Food and Drug Administration and to partly replace established clinical treatments."

More information: Marcus Mumme et al. Nasal chondrocyte-based engineered autologous cartilage tissue for repair of articular cartilage defects: an observational first-in-human trial, *The Lancet* (2016). DOI: 10.1016/S0140-6736(16)31658-0

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