

<b>Title:</b>	<b>Matrix-induced autologous chondrocyte implantation and autologous chondrocyte implantation</b>		
<b>Agency:</b>	Medical Services Advisory Committee (MSAC) MDP 853 Commonwealth Department of Health and Ageing GPO Box 9848 Canberra ACT 2601 <a href="http://www.msac.gov.au">http://www.msac.gov.au</a>		
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### **Aim**

To assess the safety, effectiveness and cost-effectiveness of matrix-induced autologous chondrocyte implantation (MACI) and autologous chondrocyte implantation (ACI) for the treatment of articular cartilage defects.

### **Results and Conclusions**

#### ***Safety***

A total of 53 studies were identified for inclusion in the assessment of the safety of MACI and ACI. This included 10 comparative studies, four comparative studies that were treated as case series, and 39 case series. Comparative studies compared MACI or ACI with microfracture, mosaicplasty or debridement. Sample sizes ranged from 10 to 309 patients, with safety data reported for an overall total of 3,254 patients.

For the majority of adverse events reported, there were no obvious differences in incidence rates between the MACI/ACI and comparator procedure groups. However one study reported that the incidence of joint swelling and joint crepitation was significantly higher following ACI compared with microfracture. Similarly, the incidence rates for joint effusion and tissue hypertrophy (both symptomatic and asymptomatic) appeared higher following MACI/ACI than following comparator procedures. Procedure failure rate was the most commonly reported adverse event, and demonstrated an incidence rate of 9.5 per cent in the MACI/ACI population, and 11.9 per cent in the comparator procedure population. Major adverse events such as joint infection and deep vein thrombosis were rare in both the MACI/ACI and comparator groups, and there were no reported deaths as a result of the procedures in either group.

Overall, the safety of MACI/ACI appears to be comparable to those comparator procedures evaluated in this assessment.

#### ***Effectiveness***

A total of 14 comparative studies were identified and included to inform on the effectiveness of MACI and ACI. A total of five randomised controlled trials (RCTs) compared MACI or ACI to microfracture (three studies) or mosaicplasty (two studies), while one pseudo-RCT compared ACI to mosaicplasty. Eight non-randomised comparative studies compared MACI or ACI to microfracture (five studies), mosaicplasty (two studies) or debridement (one study).

Functional outcomes were the focus of the majority of included studies; however, a number of studies also reported imaging outcomes following MACI/ACI and comparator procedures.

A variety of scoring systems were used to assess knee function, which made it difficult to draw direct comparisons between the different procedures across studies. The most commonly reported functional outcome measures were the Lysholm and Tegner scores. Of the eight studies that reported Lysholm scores, six reported no significant difference in the effectiveness of MACI/ACI over time compared with comparator procedures; however, one study each reported that MACI/ACI was more effective over time compared with microfracture and mosaicplasty. Similarly, of the five studies that reported Tegner scores, four studies reported no significant difference in the effectiveness of MACI/ACI over time compared with comparator procedures; however, one study reported that MACI was more effective over time compared with microfracture.

Most studies that assessed these outcomes reported that quality of life and pain scores were not significantly different following MACI/ACI compared with comparator procedures; however, one study did report that the improvement in pain scores following ACI was significantly better compared with debridement. Imaging outcomes, reported in a limited number of studies, revealed no significant difference in the quality of articular cartilage repair following MACI/ACI compared with comparator procedures. Similarly, one study reported that at five year follow-up, there was no significant difference in the frequency of radiographic changes that were indicative of osteoarthritis in MACI/ACI patients compared with patients who underwent microfracture.

Overall, in the short to medium term, the effectiveness of MACI/ACI appears to be comparable to those comparator procedures evaluated in this assessment.

### ***Cost-effectiveness***

A full economic evaluation was not undertaken because of the lack of evidence supporting the superior effectiveness of MACI/ACI. The results of the costing analysis demonstrated that MACI/ACI is more costly than either microfracture or mosaicplasty. The reason for the additional cost is two-fold. Firstly, MACI/ACI require two separate surgical procedures, the first to biopsy the chondrocyte cells and the second to implant the cultured cells. Mosaicplasty and microfracture only require a single procedure. Therefore the extra procedure has flow-on costs in terms of additional MBS items and patient co-payments. Secondly, MACI/ACI requires the isolation and growth of chondrocyte cells in tissue culture. This cost is significant and adds an extra \$11,400 per knee repaired.

Precise identification of the number of patients eligible for MACI/ACI was difficult, and two estimates were calculated. The first estimate was based on the number of patients currently undergoing hyaline cartilage repair. The second estimate was based on the potential number of patients suitable for cartilage repair, this being an estimate of the unmet demand for MACI/ACI. The financial implications were indicative only, since they assumed a 100 per cent switch from mosaicplasty or microfracture to MACI/ACI. The actual uptake rate of MACI/ACI was not estimated because of the uncertainty around this value.

Patient characteristics and damage pathology were not considered. As suggested by the Advisory Panel, the size and number of lesions may influence the preferred treatment options. Also not considered was the possibility of using MACI/ACI as a second line treatment in patients who had previously failed either microfracture or mosaicplasty.

### **Methods**

The evidence regarding the use of MACI and ACI for the treatment of articular cartilage defects was systematically assessed. PubMed, EMBASE and the Cochrane Library were searched for relevant literature from inception of the databases to March 2010. Studies were included in the review using pre-determined PICO selection criteria and reasons for exclusion were documented. The quality of studies was assessed, data were extracted in a standardised manner, and results were reported narratively.