

Marrow Stimulation - What have we learned after 60 years of drilling for answers?

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Introduction

In 2017 it will be 60 years since Smillie introduced the idea of subchondral drilling¹, followed by Pridie in 1959 who then suggested it as a treatment for Osteoarthritis.² In the 1970's Lanny Johnson, one of the grandfathers of Arthroscopy began performing abrasion arthroplasty using first generation arthroscopic burrs.³ His technique fell out of favor in the 1990's at which time Steadman introduced the concept of microfracture (MF).⁴

There are approximately 80,000 microfracture procedures performed each year in the US^{5,6}; however, the actual number could be substantially larger. In 2006, approximately 1 million arthroscopic knee procedures were performed in an outpatient setting.⁷ Widuchowski et al. found chondral lesions in 60% of 25,124 knee arthroscopies; of those, 67% were classified as localized focal osteochondral or chondral lesions.⁸ Based on these findings, it can be estimated that 40% or 400,000 knee arthroscopies each year may benefit from adjunct focal cartilage repair procedures. Due to the heterogeneity and the uncertain natural history of cartilage lesions, exact numbers remain unknown.⁸

In 2015, articles and editorials in the Journal of Arthroscopy called into question whether there was any evidence to support the continued use of microfracture. Jack Bert recommended abandoning the procedure citing a lack of improvement over debridement alone and the destruction of subchondral bone.⁹ Lanny Johnson recommended a return to abrasion arthroplasty or the use of a single puncture rasp.¹⁰

Standard of Care

Still today, almost 30 years after its introduction, microfracture remains the most popular first line marrow stimulation treatment for early cartilage damage, especially for lesions of the knee.^{5,6} The therapeutic benefit of bone marrow stimulation is mainly attributed to the role of mesenchymal stem cells (MSCs) recruited from the bone marrow¹¹, forming into a new fibro-cartilage layer over the lesion. In order to reach these marrow rich structures, several factors play an important role.

Limitations

During the past decade, the scientific interest has shifted away from viewing articular cartilage in isolation and placing more focus on the osteochondral unit.¹²⁻²¹ Advancements in microCT imaging provided new radiographic insight into the subchondral micro-architecture and the structural effects following microfracture and alternative marrow stimulation methods.^{12,15-21} Combined with new histological findings, the latest evidence outlines the significant shortcomings of standard microfracture awls and other cartilage tools. This may explain the decline in clinical outcomes between 18-36 months after the procedure.²²⁻²⁸

Channel Depth

The perforation depth of the microfracture awl ranges from 2-4mm depending on the force and how often the awl is struck.^{13,14,19} The average subchondral bone plate thickness varies by location and joint. For example, on the tibial plateau it ranges from 0.1mm to 0.9mm.²⁹ Standard microfracture depth provides limited access to the marrow rich subarticular spongiosa, especially in chronic lesions with subchondral sclerosis. Hoemann et al. reported a marrow access in human tissues that ranged from 70% (nonlesional bone) to 40% (extremely dense bone). More specifically, the authors demonstrated failed marrow stimulation with a depth of 2mm penetration into sclerotic bone.¹⁹

Channel Diameter

In 2013, Hoemann et al. demonstrated the effects of microfracture on human bone.¹⁹ The use of standard awls resulted in top hole diameters at the articular surface ranging from 1.1 to 2.0mm. Depending on the thickness of the awl, compaction damage formed in a 0.3-1.0-mm ring beyond the macroscopically visible hole, with a larger radius of fracture damage for thicker awls and deeper holes.

Subchondral Bone Effects

The effects stemming from the conically shaped microfracture awl tips have been studied extensively in recent years: In 2009, Chen et al. showed the creation of 0.2mm thick and 1mm deep sleeves of dense compacted bone surrounding MF holes both in histology and on micro-CT.¹² As a result, the holes were largely sealed off with little or no access to the bone marrow space. This was reconfirmed by several other studies.^{16,18,19} The larger footprint of the V-shaped microfracture awls (>1.5mm wide) results in crushing and fracturing of bone. This induced substantial osteocyte necrosis surrounding each hole which may explain an increased osteogenic response with the formation of intralesional osteophytes.^{12,17,18,22,24,36} The iatrogenic damage to the subchondral bone may also influence the bone bridge stability between holes and the overall structure of the repair site when the perforation density becomes too high.¹⁸ The physiological trabecular distance has to be taken into consideration when choosing non-rotational instruments to penetrate into the subchondral bone. In the ovine model, this distance is 0.9 +/-0.13mm²⁰ and human subchondral bone has been shown to correlate to the sheep model.¹⁷ When using axial force, thicker instruments that do not correspond to the trabecular distance increase the risk of bone compaction.

Treatment Standardization

In addition to the heterogeneity of cartilage repair cohorts, the variability of microfracture awls with respect to tip diameter, length, applied force, and channel density, makes comparability of treatment results difficult.¹⁸

Rehabilitation

Post-operative protocol recommendations for microfracture are varied with the standard being 6 weeks of partial weight bearing and daily use of a CPM machine for as much as 8 hours per day.³⁰ Failure to comply with post-operative requirement is a very practical consideration as non-compliant patients can compromise positive outcomes from the surgical intervention. Many patients who fit the marrow stimulation patient profile may not be ideal candidates because their life, work and activity requirements prevent them from following the recommended post-op protocol.

Solutions

Channel Depth

Results from quantitative histomorphometry and histological scoring showed that deeper marrow access resulted in more hyaline character in the repair matrix indicated by significant improvement in cartilage defect fill, increased glycosaminoglycan and type II collagen content and reduced type I collagen. Improved stimulation of cell recruitment through deeper marrow access induced a larger region of subchondral repairing and remodeling which positively correlated with improved cartilage and subchondral bone repair.^{14,15} Benthien et al. showed comparative ovine microCT imaging using a stop controlled 1mm thick needle reaching 9mm into the subchondral bone, approximately three times the channel depth of standard microfracture holes.¹⁸

Channel Diameter

In 2014, Eldracher et al. compared marrow stimulation using 1.0 or 1.8mm K-wires with rotation at a standardized depth of 10 mm in an ovine model.²⁰ Small subchondral drill holes that reflect the physiological trabecular distance significantly improved osteochondral repair in a translational model more effectively than larger drill holes. This was seen on histological matrix staining, cellular morphological characteristics, subchondral bone reconstitution, and average total histological score as well as significantly higher immunoreactivity to type II collagen and reduced immunoreactivity to type I collagen in the repair tissue compared with 1.8-mm drill holes. The micro-architecture of the subarticular

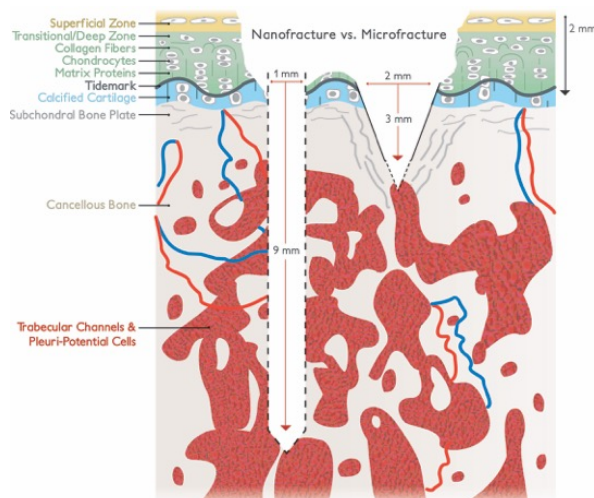


Figure 1: Comparison of Microfracture to Nanofracture. Considerations for standardized and outcome predictable cartilage remodeling: a technical note.¹⁸

spongiosa was better restored after 1.0-mm drilling with significantly higher bone volume, more and thinner trabeculae, and the bone mineral density was similar to the adjacent subchondral bone. These results were reconfirmed in a recent publication using a custom, stop-controlled, non-rotational awl (5mm deep) comparing 1.0 to 1.2mm diameters.²¹ While there were no differences on microCT among the two diameters, the histological results of the thinner awls showed a significant improvement of the overall repair tissue quality and surface grading compared to larger awls. The comparative human tissue study by Hoemann et al. reconfirmed these findings showing that thin tapered awl geometries allowed easier perforation of dense bone and produced less bone compaction.¹⁹ Similarly, the k-wires used by Eldracher et al., the custom awls used by Orth et al., and the nanofracture needles introduced by Benthien et al. showed a 1mm diameter channel on microCT extending from top to bottom.^{18,20,21}

Subchondral Bone Effects

The subchondral bone needling procedure (Nanofracture, Arthrosurface, Franklin, MA, USA) introduced by Benthien in et al. in 2013 (Figure 1) was in response to the renewed attention to the effects of subchondral bone in cartilage repair.¹⁸ The microCT in an ovine model showed multiple open trabecular channels throughout the 9mm deep subchondral bone perforation with a physiological, irregular wall outlining the channel. The trabecular bone structure appeared to have normal thickness and density.¹⁸ A custom 1mm thick awl used by Orth et al.²¹ led to a significant improvement in the overall repair tissue quality, histological surface grading, and regularity compared with larger 1.2mm awls. Both on microCT and histology, the results did not show the typical bone compaction effect reported after the use of traditional microfracture awls.^{12,16,18,19}

Treatment Standardization

Subchondral bone needling has opened new pathways for potential improvement in marrow stimulation in particular as they relate to a standardized channel formation and depth, cell recruitment, and the ensuing cartilage quantity and quality.¹⁸ Compared to the highly variable, user dependent microfracture awl, nanofracture perforation is standardized with predetermined diameter and depth.

Rehabilitation

Emerging new evidence from recent publications suggests a change in the postoperative rehabilitation may also be beneficial for cartilage repair.

Schatti et al. showed that neither compression nor shear alone was sufficient for the chondrogenic induction of human mesenchymal stem cells.³¹ However, the application of shear superimposed upon dynamic compression led to significant increases in chondrogenic gene expression without affecting hypertrophic and osteogenic markers. Other studies underlined the importance of a sliding-type biomechanical stimulus for the regeneration and maintenance of an operative articular surface.³²⁻³⁴ A skateboard style sliding motion combines shear and compression with partial weightbearing which may optimize the healing response compared to traditional CPM (Figure 2).



Figure 2: Skateboard Active Motion (SAM) Combined compression, shear, and partial weightbearing.

Patient Profile

In their systematic analysis of microfracture, Mithoefer et al. identified several outcomes predictors²⁸ that play an important role in first and second generation MSC stimulation procedures (Table 1,2).

Table 1: Patient Indicators for Improved Outcomes

Age ²⁸	<40 years
Duration of symptoms ²⁸	<12 months
Lesion size ²⁸	up to 2x2cm
Lesion depth ²⁸	<5mm
Body mass index ²⁸	<30 kg/m ²
Previous surgery ²⁸	Primary microfracture
Repair cartilage volume ²⁸	Good defect fill (>66%)
Mechanical alignment ³⁵	Normal
Joint anatomy ³⁵	Normal
Joint stability ³⁵	Ligamentous stability with adequate muscle strength
Meniscus	Normal without loss of meniscal tissue

Table 2: Comparison of MSC Access on 1st and 2nd Generation Microfracture

First Generation Microfracture	Second Generation Microfracture
Channel Depth	
<ul style="list-style-type: none"> Shallow depth of 2-4mm with limited access to subarticular spongiosa^{13,14,19} Variable force^{13,14,19} Marrow access in 40-70%¹⁹ Failed marrow stimulation in sclerotic bone¹⁹ 	<ul style="list-style-type: none"> Deeper reach 5-10mm with better marrow access, improved cell recruitment^{14,15} Stop controlled¹⁸ More hyaline character^{14,15} Significant improvement in cartilage repair^{14,15,18}
Channel Diameter	
<ul style="list-style-type: none"> ~2 mm top side¹⁹ Conical tip – larger footprint¹⁹ Thicker awl – increased compaction¹⁹ Larger radius of fracture damage¹⁹ 	<ul style="list-style-type: none"> 1mm top to bottom^{18,20,21} Needle tip – smaller footprint Less compaction¹⁹ Less fracture damage^{20,21}
Subchondral Bone Effects	
<ul style="list-style-type: none"> Bone compaction causing sealing/sleeve effect^{12,16,18,19} Increased osteocyte necrosis^{12,17,18} Osteogenic response^{12,17,18} Intralesional osteophytes^{12,17,18,22,24,36} 2mm instruments do not correspond to physiological trabecular distance^{17,20} 	<ul style="list-style-type: none"> No sealing/sleeve effect^{12,16,18,19} Open channel access to bone marrow¹⁸ 1mm instruments better match the physiological trabecular distance¹⁸

Conclusions

The use of standard microfracture awls is no longer supported by recent basic science evidence^{12,14-21} which seems to concur with Jack Bert's entreaties.⁹ In fact, the widely described subchondral bone compaction effect may be counterproductive to its intent of MSC recruitment. Throughout the basic science literature, thinner and deeper access that avoids bone compaction and maximizes MSC recruitment while at the same time minimizing the iatrogenic injury to the subchondral bone, has been described as superior. With the increasing need for an inexpensive, simple and reproducible first line cartilage treatment, the 2nd generation microfracture needling techniques may offer an attractive alternative. Future clinical series are necessary to confirm the preclinical findings while validating the new instrumentation and rehabilitation pathways.

Key Words

Indications: Cartilage Lesion, Focal Chondral Defect

Procedures: Cartilage Repair, Bone Marrow Stimulation, Mesenchymal Stem Cells, Microfracture, Nanofracture

Joints: Knee

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