# Clinical Intelligence

## Cartilage Repair and Regeneration

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# Cartilage Repair and Regeneration

Treatment of symptomatic articular cartilage defects of the knee has evolved tremendously in the past decade, and it continues to improve and expand. Articular cartilage has a limited healing capacity, allowing few treatment options for patients who suffer from either partial-thickness or full-thickness cartilage lesions. In the past, patients often were treated symptomatically until they became eligible for osteotomy or total joint replacement (TJR). Today, reparative and restorative procedures are being developed to address this significant source of morbidity in young, active patients. Procedures have been developed, not only to alleviate the symptoms associated with articular cartilage defects, but also to limit progression of isolated cartilage lesions into degenerative arthritis.

Cartilage repair and regeneration (CRR) surgical techniques are not ready for widespread adoption and do not represent standard orthopedic care. CRR techniques can help orthopedics programs achieve market differentiation and a first-mover advantage, but currently these procedures should be performed by only a select number of surgeons treating a limited group of patients.

In the short term, CRR procedures will evolve to better address traumatic cartilage defects, while in the long term, they will be developed to treat early-stage osteoarthritis (OA).

**Key Facts**

- More than 45 million people in the US currently have osteoarthritis.
- Over 15 million OA patients require medical or surgical treatment.
- Arthritis prevalence is expected to grow to 50 million by 2010 and 64 million by 2030.
- More than 7 million sports-related injuries occur in the US each year, resulting in more than 2.6 million arthroscopy surgical procedures annually.
- CRR techniques are currently limited to treating traumatic cartilage defects of the knee. The scope of treatment is expanding to other anatomical joints in the short term and to degenerative defects in the long term.
- 2,000 to 3,000 cartilage repair procedures are performed in the US each year.

**Cartilage Repair and Regeneration: Strategies for Success**

- Evaluate program capabilities and strengths.
- Identify current market offerings and potential opportunities.
- Assess advantages and challenges.
- Evaluate surgeon and institution appetite for emerging technology.
- Develop quality assurance and continuous improvement matrices.
- Enhance stakeholder communication.
- Capitalize on upstream and downstream interventions.
- Collaborate with select physicians.

*Cartilage Repair and Regeneration* underscores the scope of the articular cartilage defect problem and explores current treatment options and concerns about inappropriate use of evolving therapies. It also highlights the strengths and limitations of new technologies, as well as future trends. Strategic adoption considerations of these technologies are emphasized to encourage smart growth.

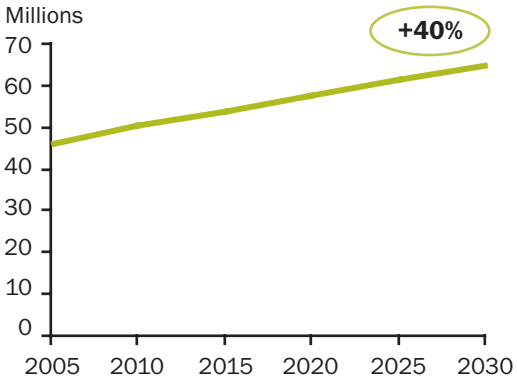
# Degenerative/Traumatic Cartilage Defects Are Increasing

As the prevalence of arthritis grows, the demand for inpatient (IP) and outpatient (OP) treatment options will likewise grow. Articular cartilage defects (chondral and osteochondral) are generally caused by either mechanical injury or metabolic diseases. Degenerative changes typical of osteoarthritis result, causing pain and impairing function, ultimately requiring medical and/or surgical treatment.

## Articular Cartilage Defects and Arthritis Prevalence Are Increasing

As the aging population grows, arthritis prevalence will increase, driving the demand for medical and surgical treatments.

**Projected Growth of Osteoarthritis Prevalence**
**US Market, 2005–2030**




| 2005 US Market | |
|---|---|
| OA Prevalence Estimate | 45.0 million |
| OA Diagnosed Population | 24.5 million |
| Medical Treatment | 14.5 million |
| Joint Replacement (knee and hip) | 800,000 |

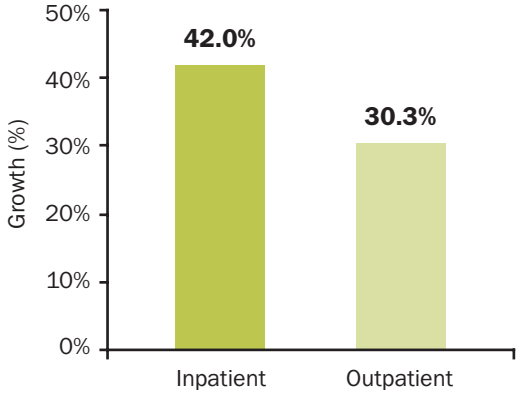
## Surgical Intervention Will Increase

Surgical treatment of traumatic and degenerative cartilage defects will increase significantly, affecting inpatient and outpatient utilization.

**Key Procedures Driving Growth**

- MIS total joint replacement
- Alternatives to total joint replacement
  - — Unicompartmental, bicompartmental knee replacement, patellofemoral replacement
  - — Hip resurfacing
  - — Shoulder resurfacing
- Arthroscopy procedures
- Cartilage repair and regeneration procedures
- Meniscal allografts
- Osteochondral allografts
- Osteotomy

**IP/OP Growth for Joint Procedures**
**US Market, 2006–2016**




MIS = minimally invasive surgery.
Sources: Impact of Change® v5.0; NHDS; Pharmetrics; HCUP; CMS; CDC; Sg2 Analysis, 2006.

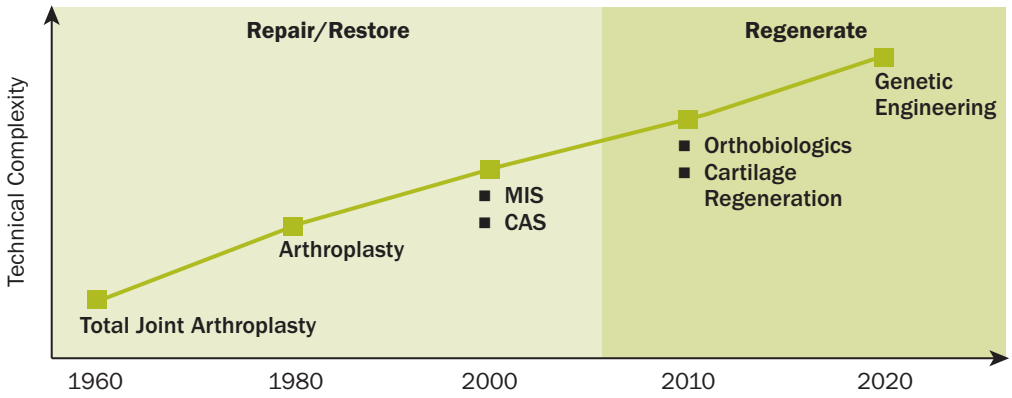
# Surgical and Regenerative Joint Care Is Evolving

Surgical treatment is expanding beyond reparative or restorative approaches. Patients with degenerative or traumatic cartilage defects were previously not treated until they became candidates for osteotomy or total joint replacement.

## Treatment Is Moving From Reparative to Regenerative

Treatment options will begin to expand for both traumatic and degenerative cartilage defects. Future treatment options will initially be more complex, but technology will be diffused more rapidly when it moves beyond the early adopter stage.

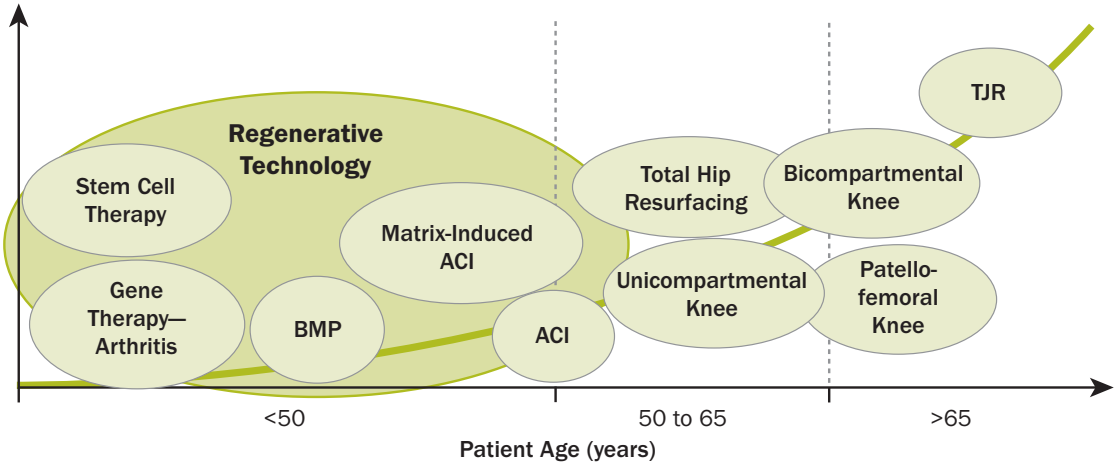
### Emerging Surgical Treatment Options




## Interventions Treat Disease Earlier in Its Progression

Procedures will be initiated earlier, expanding the treatable patient population and increasing the number of treatment episodes.

### Treatment Options for Joint Patients




ACI = autologous chondrocyte implantation; BMP = bone morphogenetic protein; CAS = computer-assisted surgery.

# Few Options Currently Repair and Regenerate Cartilage

Current treatments for defective articular cartilage relieve symptoms, remove mechanical irritants or rely on the body's natural process to self-repair and regenerate. These procedures are quick, safe and technically easy to perform, but they provide only temporary relief and lack appropriate tissue fill and integration.

**Established Treatment Options for Articular Cartilage Repair**

| Palliative | Advantages | Challenges |
|---|---|---|
| **Viscosupplementation**<br>Injection of hyaluronic acid into the joint to replace/supplement synovial fluid | ■ Shock absorption and lubrication restored<br>■ Maintenance of boundary layer around pain receptors reduces pain<br>■ Cost effective | ■ Provides only temporary relief<br>■ Requires 3 to 5 injections<br>■ Only alleviates symptoms<br>■ Does not treat pathophysiology |
| **Debridement and Lavage**<br>Removal of injured cartilage, fibrin debris and inflammatory mediators | ■ Quick<br>■ Safe<br>■ Cost effective<br>■ Reduction of surface debris and mechanical symptoms | ■ Provides only temporary relief<br>■ Lacks tissue fill and integration<br>■ Does not repair the joint damage itself, but alleviates clinical symptoms |
| **Intrinsic Repair Stimulus** | **Advantages** | **Challenges** |
| **Mesenchymal Stem Cell (MSC) Stimulation**<br>Recruitment of mesenchymal stem cells to site of injured cartilage for purpose of forming repair tissue (eg, microfracture, drilling) | ■ Technically easy<br>■ Single-stage<br>■ Cost effective<br>■ Arthroscopic<br>■ Tissue fill | ■ Introduces tissue fill unpredictably<br>■ Presents potential for bony overgrowth<br>■ Offers limited durability and high reoperation rate<br>■ Applies only to small lesions<br>■ Grows fibrocartilage<br>■ Requires crutches (extended recovery) |

# Advanced Procedures Are Early in Their Development and Adoption

As repair and regeneration techniques advance, alternative approaches range in both effectiveness and complexity. Treatments continue to develop from cell-based repair to whole-tissue repair and stem-cell–based therapies. These emerging technologies have limited long-term outcomes data for efficacy and cost effectiveness.

**Emerging Treatments for Articular Cartilage Repair**

| Cell-Based Repair | Advantages | Challenges |
|---|---|---|
| **Autologous Chondrocyte Implantation**<br>Implantation of cartilage cells previously harvested from the patient, grown in-vitro and reimplanted into defective areas to form hyaline-like repair tissue (eg, periosteal patch, collagen, matrix-induced) | ■ Autologous modality, eliminating risk of rejection and disease transmission<br>■ Hyaline-like tissue<br>■ Appropriate for larger lesions<br>■ No need for containment<br>■ Good peer reviewed study results | ■ Technically demanding<br>■ Staged surgery<br>■ High cost<br>■ High reoperation rate (20% to 50%)<br>■ Extended recovery period<br>■ Documented donor site morbidity |
| **Whole Tissue-Based Repair** | **Advantages** | **Challenges** |
| **Autologous Osteochondral Transplantation**<br>Implantation of fully formed cartilage construct harvested from the patient for the purpose of resurfacing the site of injury with hyaline cartilage (eg, mosaicplasty, OATS) | ■ Hyaline cartilage<br>■ Quick recovery<br>■ Cost effective<br>■ Appropriate for uncontained lesions | ■ Technically demanding<br>■ Limited donor tissue—lesions must be smaller<br>■ Documented donor site morbidity<br>■ Imprecise contour; long-term effects unknown<br>■ No interface integration |
| **Allograft Osteochondral Transplantation**<br>Implantation of fully formed cartilage construct harvested from a donor for the purpose of resurfacing the site of injury with hyaline cartilage | ■ Hyaline cartilage<br>■ Good fill<br>■ Viability potential<br>■ Durability<br>■ No donor site morbidity<br>■ Appropriate for large lesions | ■ Disease transmission risk<br>■ Potential for bony healing<br>■ High cost<br>■ Limited availability<br>■ Potential for immune reaction<br>■ Compromised material properties |
| **Stem-Cell–Based Therapies**<br>Implantation of multipotent stem cells, which can self-renew and repair and regenerate tissue | ■ Unlimited cell replication<br>■ Good fill and integration with healthy cartilage | ■ Development in early stages<br>— Beginning exploration in humans, particularly in bone and spinal disc regeneration |

OATS = osteochondral autograft transfer system.

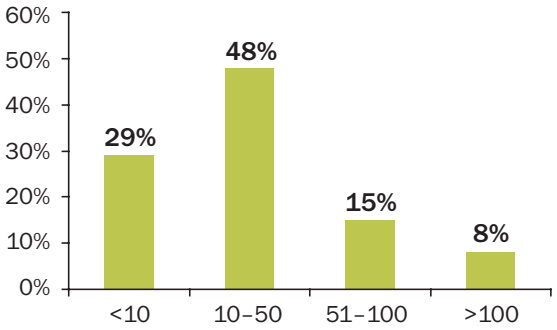
# Emerging Techniques Are Limited to Select Surgeons/Centers

Emerging cartilage regeneration surgical techniques are not ready for widespread adoption and currently do not represent the standard of orthopedic care. Both procedure cost and long-term efficacy remain barriers to greater adoption.

## Current Treatment Options Are Limited

While current developments are heavily centered on treating patients with traumatic cartilage defects in the knee, continuing progress will expand utilization to other anatomical joints, and ultimately, to degenerative indications. Most surgeons perform only a limited number of cartilage repair procedures per year.

**Number of Cartilage Repair Interventions Performed by Surgeons per Year International Market, 2006**

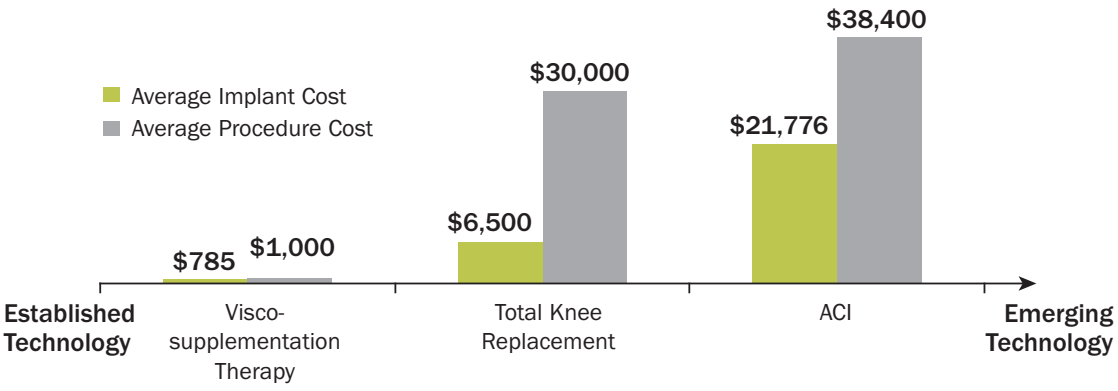



77% of surgeons trained in cartilage repair techniques perform less than 1 procedure per week.

## Cost and Procedure Complexity Narrow Widespread Adoption

While current indications limit patient eligibility, the physician learning curve for cartilage regeneration is significant. Implant and overall procedure costs are significantly higher for cartilage regeneration procedures than currently established technologies. Long-term outcomes data on cartilage repair and regeneration are lacking.

**Average Wholesale and Procedural Costs per Implant/Unit, 2006**



# Long-Term Outcomes Data for Current Techniques Are Lacking

While cartilage repair and regeneration technology continues to evolve and outcome studies are under way, current research leaves many unanswered questions. Improved efficacy has not been shown. Moreover, the durability of these techniques and the extent to which they prevent the development of osteoarthritis and reduce the need for knee replacements remain critical issues for further research.

## Advanced Techniques Have Yet to Show Superior Outcomes

Despite the recent developments of advanced reparative and regenerative techniques, there are no long-term studies that clearly show treatment effectiveness.

**Randomized Clinical Trials of Cartilage Repair/Regeneration**

| Author/Year | Patient Population | Duration | N | Conclusions |
|---|---|---|---|---|
| **Bachman et al. 2004** | mACI vs microfracture | 1 to 2 years | 46 | ■ The study demonstrated the feasibility of the mACI technique.<br>■ The process requires 2 years for full-thickness cartilage to be produced after ACI. |
| **Knutsen et al. 2004** | ACI vs microfracture | 2 years | 80 | ■ Only small differences in outcomes were observed at 2 years.<br>■ The microfracture group had significantly more improvement in the preoperative physical component score (SF-36) than the ACI group. |
| **Horas et al. 2003** | ACI vs transplanted osteochondral cylinders | 2 years | 40 | ■ Recovery of ACI patients was significantly worse on functional knee scoring, but not on other outcome indicators. |
| **Bentley et al. 2003** | ACI vs mosaicplasty | 19 months | 100 | ■ Good or excellent outcomes were achieved in 88% of the ACI patients and in 69% of the mosaicplasty patients (NS).<br>■ Conflict of interest evidence was presented. |

mACI = matrix-induced autologous chondrocyte implantation; NS = not significant.
Sources: Bachman et al. *Radiologe* 2004;44:773–782; Knutsen et al. *J Bone Joint Surg Am* 2004;86-A(3):455–464; Horas et al. *J Bone Joint Surg Am* 2003;85-A(12):2487–2488; Bentley et al. *J Bone Joint Surg Br* 2003;85(2):223–230; Sg2 Analysis, 2007.

# Next-Generation Techniques Offer Promise

First-generation therapies offer marginal solutions for dealing with articular defects. The lack of superior outcomes is further complicated because most cases of cartilage defects result in progressive degeneration. Next-generation advancements in ACI techniques have the potential to reduce morbidity and improve outcomes.

## ACI Is Still Early in Its Development

**2012–2015**
**Third-Generation ACI**
The technology is 100% autologous and involves no synthetic, human or animal-based donor material. Chondrocytes are seeded in collagenic spheroids and injected by a syringe in a single step.

**2009–2011**
**Second-Generation ACI**
The first-generation, autologous periosteal patch is replaced by the suspension of chondrocytes in a synthetic/animal/human 3D matrix. This reduces the number of donor grafts and graft sites needed and permits less invasive, arthroscopic approaches.

**2006–2007**
**First-Generation ACI**
Healthy chondrocytes are harvested, cultured in the laboratory and reintroduced to the patient in a liquid-based suspension. Soft tissue is harvested to produce a periosteal patch, which provides a water-tight environment.

## Second-Generation ACI Techniques Seem More Promising

Cell- and whole-tissue–based approaches are the only procedures that replenish the defect in the long run with either actual or near-actual cartilage tissue. The indisputable advantages of these strategies are being combined with tissue engineering refinements and surgical advancements.

**Autologous Chondrocyte Implantation**

| First-Generation ACI Challenges | Second-Generation ACI Advantages |
|---|---|
| ■ Complex, invasive and costly | ■ 1-step process |
| ■ Technically challenging procedure | ■ Reduced surgical morbidity |
| ■ Relatively high revision rates (20% to 50%) | ■ Better cell maturation through improved suturing and biodegradable scaffolds |
| ■ Lack of new cartilage integration | ■ Mini-incision and arthroscopic approaches |

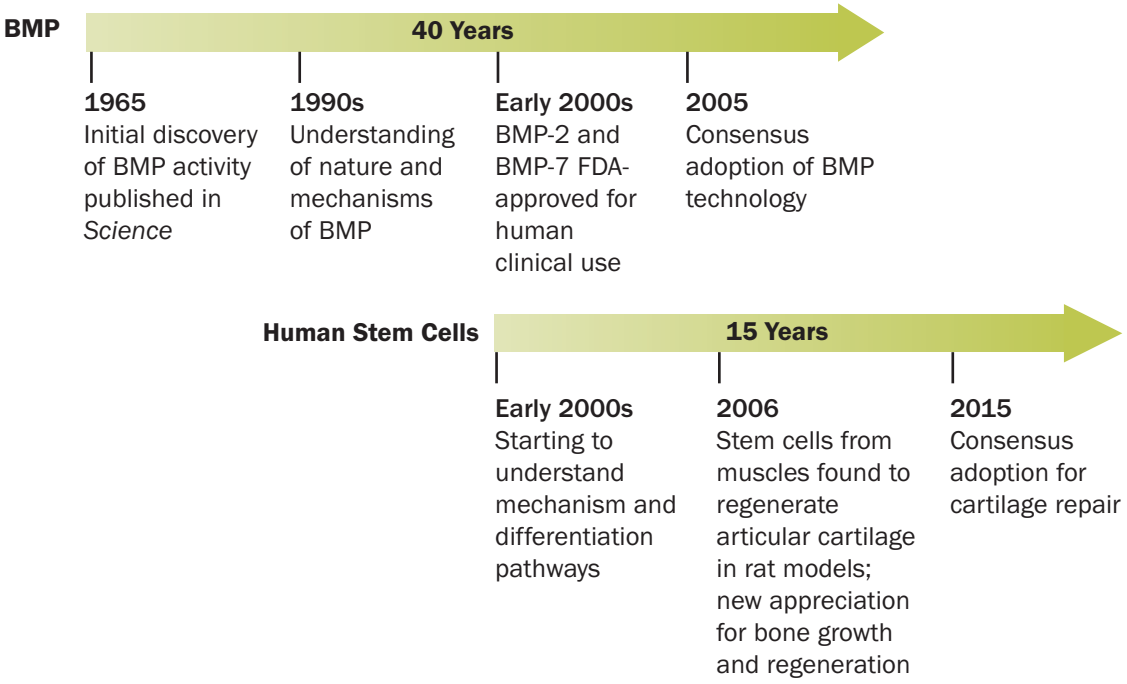
 

# Stem Cells Will Provide the Next Level of Care

Stem cells isolated from mesenchymal tissues have the potential to address many of the shortcomings of current techniques. These techniques have the theoretical advantage of providing unlimited numbers of cells, thereby reducing the number of surgeries required to harvest autologous tissue and their associated complications. While current research is promising, these approaches are 8 to 10 years away from becoming significant clinical applications.

## Stem Cell Products Are Following BMP's Evolution

Stem cell products for cartilage repair will likely follow a similar adoption path as orthobiologics. Currently, these products are in an early stage of development, similar to where bone morphogenic protein technology was in the early 1990s. Over time, clinical effectiveness will increase while cost will decrease.




**Advantages and Challenges to Stem Cell Adoption**

| | |
|---|---|
| **Advantages** | ■ Short window before it can become a commodity product<br>■ Less technically challenging with a short physician learning curve<br>■ Less device-dependent |
| **Challenges** | ■ Non–standard-of-care technologies face different payer model<br>■ New imaging and diagnostic requirements needed<br>■ Government regulation to impact adoption |

# Diagnostic Protocols and Technologies Are Emerging

Advancements in imaging technologies and protocols permit earlier noninvasive diagnosis and monitoring of cartilage damage. Molecular-based diagnostics also will expand the boundaries of detection and monitoring for "at-risk" groups.

## Diagnostic Protocols Will Move Beyond Conventional Imaging Techniques

New diagnostics will permit better tracking of both degenerative and regenerative processes.

| Current Diagnostic Modalities | Emerging Cartilage-Specific Diagnostic Modalities |
|---|---|
| **Static Assessment**<br>■ X-ray<br>■ Magnetic resonance imaging (MRI) | **Morphologic Assessment**<br>■ MRI quantitative T2 mapping<br>— Detects changes in cartilage water content (early OA has high water content)<br>— Provides information about the structural integrity of the collagen matrix<br>■ T1 mapping with delayed gadolinium (enhanced MRI)<br>— Helps identify regions of proteoglycan loss<br>— Provides equilibrium partitioning of an ionic contrast agent microCT (EPIC-microCT)<br>— Provides 3D color-coded cartilage mapping<br>■ High-resolution imaging with contrast agent<br>— Provides equilibrium partitioning of an ionic contrast agent microCT (EPIC-microCT)<br>**Disease-Specific Biomarkers** |

## Morphologic Assessment Will Enhance Diagnostic Capabilities

Current and near-future advancements go beyond imaging of cartilage morphology and will be able to noninvasively assess cartilage biochemistry. This will improve the ability to detect early cartilage injury and wear, assess suitability for cartilage repair and monitor postoperative status.

**T2 Mapping Enhances the Ability to Evaluate and Monitor Cartilage Defects and Repair**

| MRI T2 Mapping | |
|---|---|
| **Advantages** | ■ It positively correlates with early molecular changes of osteoarthritis.<br>■ It differentiates varying degrees of cartilage pathology.<br>■ It can evaluate surgical candidates slated for procedures aimed at delaying the progression of osteoarthritis.<br>■ It provides insight into the ultrastructure of surgically manipulated cartilage at the repair site and in the adjacent cartilage. |
| **Challenges** | ■ Cartilage architecture itself can often skew T2 maps, misreporting the presence and extent of tissue defects.<br>■ Noninvasive (MRI) assessment of cartilage matrix is still under development. It requires further validation and application to longitudinal clinical studies.<br>■ Studying the impact of new technology on slowly progressing disease and comparing the results to pre-existing treatments take decades. |

EPIC-microCT = equilibrium partitioning of an iconic contrast agent microcomputed tomography.

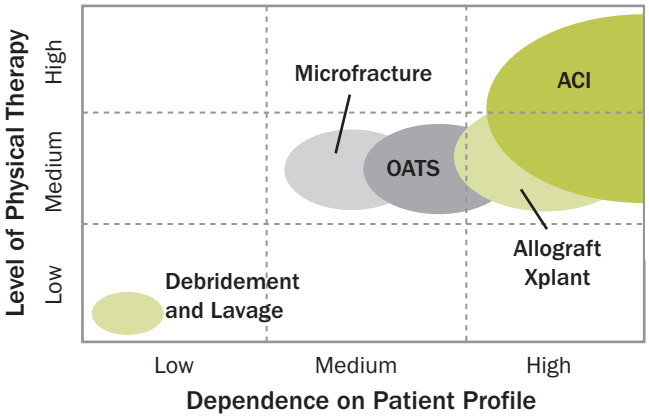
 

# New Rehabilitation Protocols Will Augment Surgery

The increasing complexity of surgical interventions requires procedure-specific rehabilitation protocols. Emerging protocols for CRR are becoming longer and more demanding for patients and providers. They are key to successful recovery and the return to full activity.

## Emerging Rehabilitation Protocols Vary in Length and Complexity

Advanced surgical options entail longer, more rigorous rehabilitation protocols that are dependent on the surgical procedure and the patient's levels of fitness and function.




- Size of circle indicates relative time in months required for pain relief and restoration of function.
- The "patient profile" includes body mass index (BMI), fitness and activity levels, and other health-related factors pertinent to the patient's intrinsic ability to recover.

## Rehabilitation Protocols Are Procedure-Specific

The type of surgical procedure performed helps determine a patient's rehabilitation regimen and recovery time.

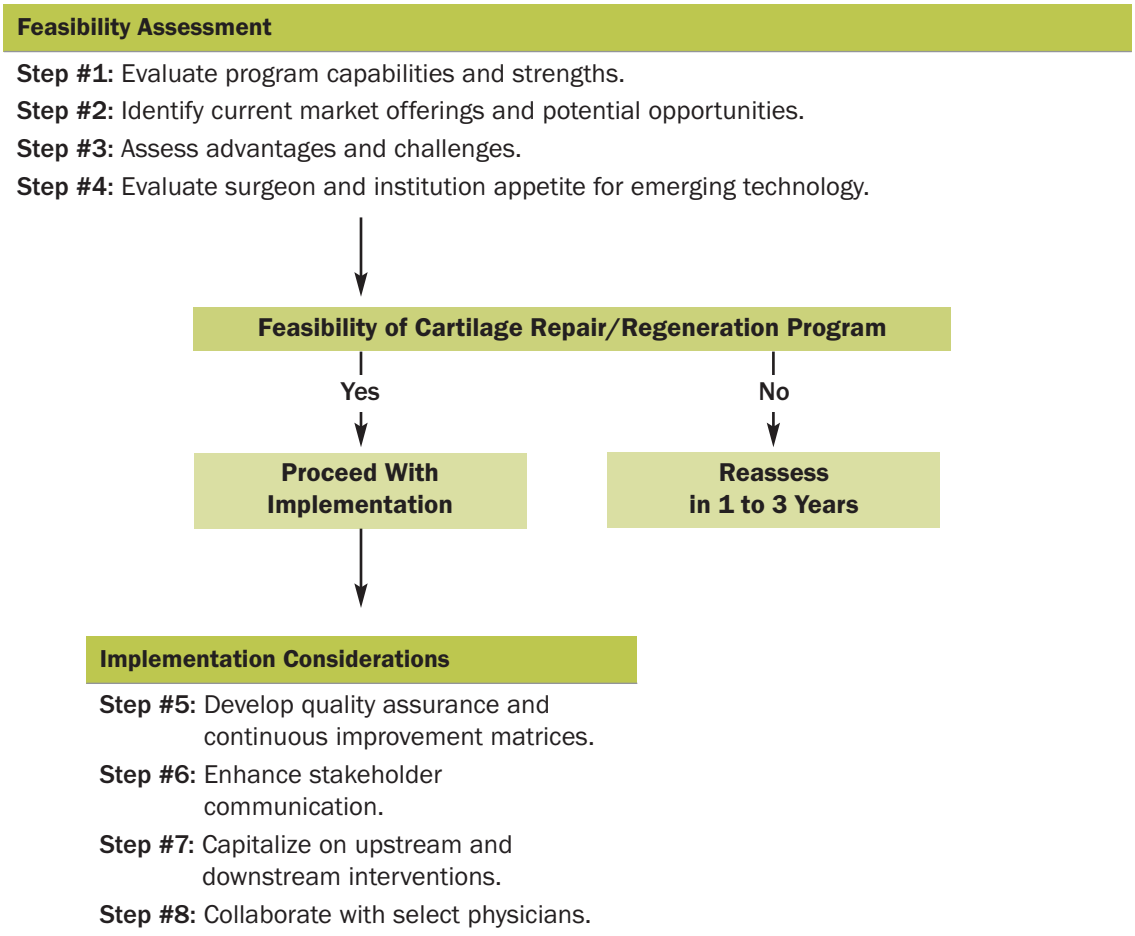
**Rehabilitation Protocols for CRR Procedures**

| Surgical Procedure | Rehabilitation Requirements | Recovery Time |
|---|---|---|
| **Viscosupplementation** | ■ Crutches not necessary<br>■ Physical therapy immediately postprocedure | ■ Short recovery time<br>■ Full weight-bearing and unrestricted activities |
| **Debridement & Lavage** | ■ Minimal crutch use<br>■ Rehab immediately after surgery<br>■ Regular activities within 4–6 weeks | ■ Short recovery time<br>■ Immediate full weight-bearing and unrestricted activities |
| **Microfracture** | ■ No weight-bearing for 6–8 weeks<br>■ Use of continuous passive motion (CPM) and pool therapy<br>■ Regular activities resume in 3–6 months | ■ 6 months to full, pain-free activity |
| **Autologous Chondrocyte Implantation** | ■ Crutches/touch-down weight-bearing at 6 weeks; full weight-bearing at 12 weeks<br>■ Pool therapy and bicycling at 6 weeks<br>■ Range-of-motion exercises/CPM used for 6 weeks<br>■ Return to sports 12–15 months | ■ 12–18 months for pain relief and restoration of function |

# Cartilage Repair Offers Differentiation but Is Not for Everyone

Narrow indications, the skill of providers, facilities and cost barriers create challenges for CRR adoption. These surgical innovations are certainly not appropriate for all orthopedics programs. Adoption of these alternatives requires rigorous decision analysis that takes into account the "costs" of innovation, learning curve progression and the likely economic return on adoption.

## Successful Adoption of CCR Requires Evaluation, Education and Integration



Step #1

# Evaluate Program Capabilities and Strengths

Effective adoption of CRR technology requires a focus on institutional core competencies and support. Although achieving organizational competence in all these components is ideal, it may not be essential in every market.

## Assess Alignment With 5 CRR Criteria

**CRR Essential and Nonessential Criteria**

| Comprehensive and Innovative Care | Market Recognition | Local Sports Affiliation | University Affiliation | Strong Research |
|---|---|---|---|---|
| **Essential** | **Essential** | **Preferred** | **Not Essential** | **Not Essential*** |
| ■ Innovative and integrated TJR and sports medicine programs<br>■ Ability to treat all grades of defect (Grades I–IV)<br>■ Rigorous patient selection protocol<br>■ Patient education<br>■ Postoperative physical therapy/rehab program<br>■ Outcome tracking | ■ Brand recognition<br>■ Physician retention<br>■ Enhanced orthopedics program image | ■ Volume driver<br>■ Credible/ reputable endorsement<br>■ Targeted patient marketing | ■ Halo effect<br>■ Teaching program<br>■ Extensive ancillary services | ■ Continued development of a nascent technology/ technique<br>■ Grant support |

**Case Study: Cartilage Restoration Center at Rush (Chicago, IL)**

- **Comprehensive and Innovative Care**
  - — The number one center for CRR in the US (accounts for 30% of all procedures)
  - — Treatment: cartilage-related pain of the knee, shoulder, elbow, hip and ankle
    - Debridement and microfracture; osteochondral autograft transplantation; osteochondral allograft transplantation; ACI; meniscus allograft transplantation
  - — Traditional procedures: unicompartmental and total knee replacement
- **University Affiliation**
  - — Rush University Medical Center; Midwest Orthopaedics at Rush
  - — Physician champion: Brian Cole, MD, MBA, Medical Director
- **Strong Research**
  - — Knee: collagen meniscus implantation; tissue engineering using chondrocytes; radiofrequency energy (RFE) impact on tissue; cartilage stiffness testing; mild degenerative changes in cartilage
  - — Shoulder: arthroscopic rotator cuff repair; radiofrequency energy; normal shoulder function
  - — Team: PhD/master scientists in biomechanics, biochemistry and anatomy; orthopedic surgeons
- **Local Sports Affiliation**
  - — Chicago Bulls; Chicago White Sox; Chicago Rush (arena football)
- **Keys to Success**
  - — Multidisciplinary team—surgeons, scientists, rehab specialists, insurance specialists
  - — Patient education and expectation management
  - — Physician education: 60% to 70% of referrals come from other orthopedic surgeons
  - — Operational efficiency and pain management

*Strong research is essential in the short term to develop new protocols and well-designed clinical studies, but it will become less essential as the technology matures.

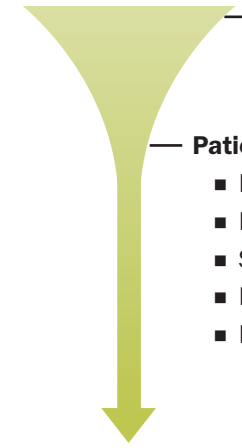
Step #2

# Identify Current Market Offerings and Potential Opportunities

Deciding whether to adopt cartilage repair strategies now or in the future requires an understanding of the local, regional and sometimes national competitive landscape, as well as the potential for program differentiation. In the short term, it's necessary to assess patient demographics and treatment options for cartilage defects in the surrounding market to pinpoint any gaps in clinical care or product variety. In the long term, programs need to understand national and international markets as medical tourism expands.

## Assess Market Opportunity

Determining patient eligibility and demand is a critical first consideration for adoption. Alternative approaches to cartilage repair are certainly not for everyone. Since CRR techniques are generally more applicable to younger, active patients, a sound evaluation of the potential patient base should focus on this athletic subset.



**Total Market Demand Potential**

CRR Potential Demand = (7% to 11%) × (# of arthroscopies in market)

**Patient-Specific Requirements**

- Patient age: <50 years old
- Patient comorbidities: previous surgery
- Size of lesion: 2–4 $cm^2$
- Location of lesion: medial condyle of knee
- Patient demand/expectations

**Total Local Market Size**

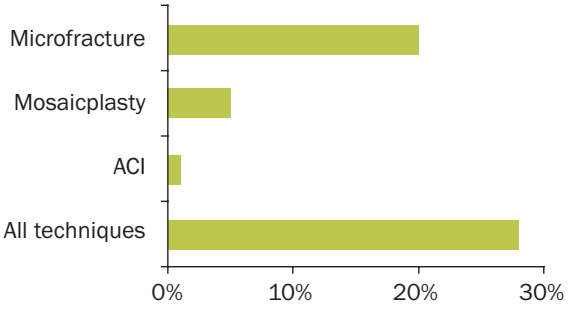
**Example: US Market**

7% of 1.8 million arthroscopies per year = 126,000 CRR potential demand per year

## Assess Market Competition

Surgeons are increasingly becoming trained in ACI and other alternative procedures. Techniques offered in each market vary, creating opportunities for differentiation.

**Techniques Offered by Surgeons Performing More Than 10 Cartilage Repair Interventions per Year International Market, 2006**




Sources: *Am J Sports Med* 2004; *Arthroscopy* 2002; Verdonk et al. 6th Symposium of the International Cartilage Repair Society (ICRS). 2006; San Diego, CA; Sg2 Analysis, 2007.

Step #3

# Assess Advantages and Challenges

Proper assessment of a CRR program requires an understanding of the myriad of factors that define this technology's demands, promises and limitations, as well as the relevance of these factors in your market.

**Cartilage Repair and Regeneration Program Considerations**

| Stakeholder | Considerations | Advantages | Challenges |
|---|---|---|---|
| **Provider** | Program development | ■ Market recognition and first-mover advantage | ■ Narrow subset of patients<br>■ Effective integration into a strong sports medicine program required |
| | Therapeutic/ procedural cost | ■ No operating room redesign needed | ■ Expensive procedures ($38,000 per procedure)<br>■ Further costs associated with more demanding rehabilitation and physical therapy regimens |
| | Technical difficulty | ■ Variable technical complexity<br>■ More widespread techniques | ■ Staged surgeries possibly required, depending on the approach<br>■ Heavily dependent on staffing and program capabilities to support surgeon |
| | Ancillary services | ■ Increased ancillary revenues and volumes | ■ Increased need for advanced imaging and rehabilitation teams |
| **Payer** | Payer contracting and billing | ■ Potential source of additional revenue and profit | ■ Precertification required<br>■ Negotiation necessary for adequate reimbursement |
| **Patient** | Efficacy | ■ Pain relief<br>■ Restoration of function<br>■ Slowing or prevention of disease progression | ■ High reoperation rates (ranging from 20% to 50% for ACI)<br>■ Long rehabilitation times |
| | Cost effectiveness | ■ Typically adopted for workers' compensation first | ■ Expensive: significant direct and indirect cost<br>■ Extensive time off work<br>■ Limited physical activity<br>■ No reimbursement from most private payers |

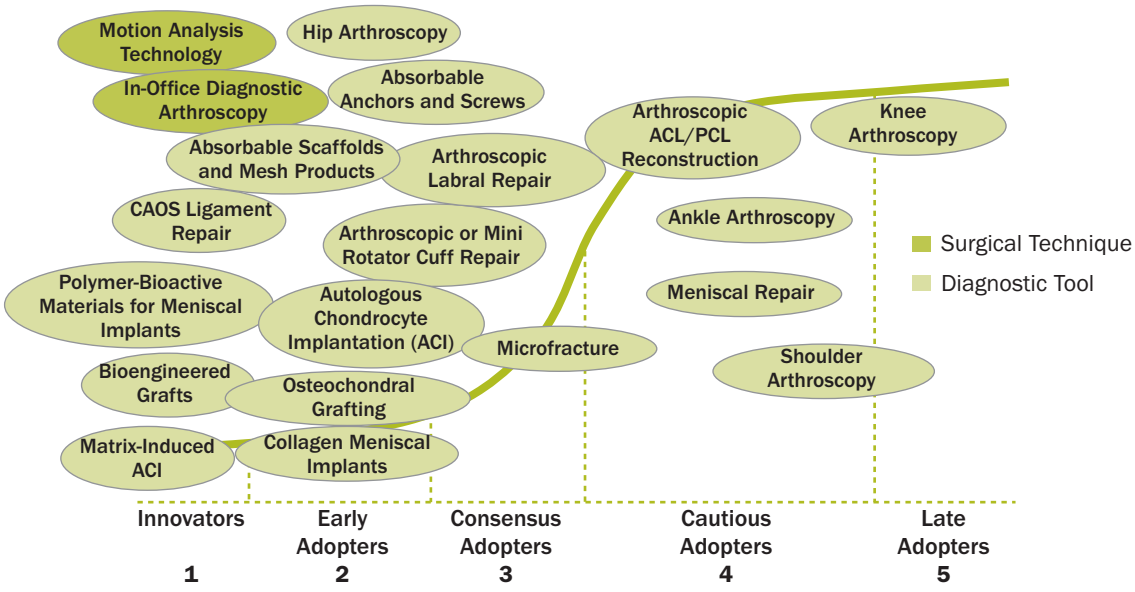
Step #4

# Evaluate Surgeon and Institution Appetite for Emerging Technology

Building an effective and successful cartilage repair program depends not only on intrinsic institutional capabilities and market demand, but also on the program's innovation synergy with an organization's existing strategy and technology adoption profile.

## Successful Programs Require Physician/Institution Readiness for Innovation

CRR Technology Adoption*




## Operation and Care Delivery Capabilities Must Be Considered

Institutions must assess their technology inventory, but they also need to understand how the advancements are integrated within the whole continuum of care. Organizations should evaluate the operational and care delivery capabilities needed to support new approaches.

Operational and Care Delivery Requirements

| | Examples | Additional Details |
|---|---|---|
| **Preoperative** | ■ Detailed patient evaluation and treatment protocols<br>■ Patient communication and education<br>■ Anesthesia | ■ Lesion location and size<br>■ Patient comorbidities<br>■ Regional (spinal) blocks<br>— Decreased hypotension and nausea<br>■ Integration and education of certified registered nurse anesthetists (CRNAs) |
| **Postoperative** | ■ Recovery<br>■ Pain management<br>■ Discharge protocol<br>■ Rehabilitation/physical therapy | ■ OP-staged procedure<br>■ Pre- and postoperative pain ladder<br>■ Catheters and continuous nerve blocks<br>■ Customized discharge orders and weight-bearing regimens<br>■ Procedure-specific protocols |

*Sg2 Technology Evaluation and Planning (STEP™) tool.
CAOS = computer-assisted orthopedic surgery; ACL/PCL = anterior/posterior cruciate ligament.

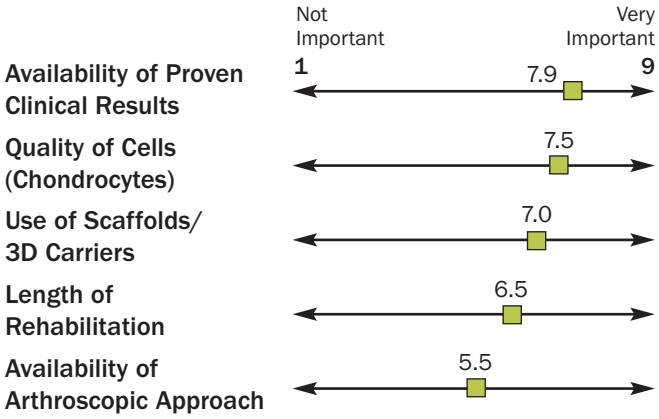
Step #5

# Develop Quality Assurance and Continuous Improvement Matrices

## Determine Keys to Success to Ensure Proper Procedure Adoption

For CRR techniques, the availability of evidence-based medical data from proven clinical results is limited. Elements crucial to the success of a procedure need to be considered individually to ensure superior outcomes.

**Case Example: ACI—Elements for Successful Cartilage Repair**




**Surgical and General Factors Determining Success**

- Patient selection
- Patient motivation
- Surgical technique
- Adherence to appropriate rehabilitation

## Develop Outcome Measures

Outcome measurement and reporting will be necessary for program assessment and communication with patients, payers and referring physicians.

**Outcome Measure Parameters**

| Outcome Type | Parameters |
|---|---|
| **General outcome indicators** | ■ Complication rates<br>■ Readmissions<br>■ Infection rates<br>■ Medical/surgical errors |
| **Composite assessment of physical state** | ■ SF–36<br>■ Western Ontario and McMaster University Osteoarthritis Index (WOMAC)<br>■ Visual analog score (VAS) |
| **Assessment of patient experience** | ■ Patient satisfaction<br>■ Functional status score<br>■ Return to work/function |
| **Other** | ■ Improved pain, symptoms and function<br>■ Rebuilt hyaline cartilage<br>■ Prevention of early OA development<br>■ Delayed arthroplasty |

Source: Verdonk et al. 6th Symposium of the ICRS. 2006; San Diego, CA.

Step #6

# Enhance Stakeholder Communication

Direct communication with patients, referring physicians, payers and employers is essential for program success. Other orthopedic surgeons currently represent the largest referral base for CRR procedures. Programs should highlight the whole continuum of care and emphasize the role of cartilage repair procedures within this paradigm.

## Communication Facilitates Stakeholder Integration Across the Continuum of Care

**Communication Strategies by Stakeholder Type**

| Patients | Referring Physicians |
|---|---|
| ■ Highlight your sports medicine program, physician practice capabilities and various treatment options.<br>— Use print media, television and Internet resources.<br>■ Conduct general seminars on articular cartilage defects and specific education programs highlighting various CRR techniques.<br>■ Develop and deploy satisfaction surveys for all sports medicine patients.<br>— Analyze results and communicate them to the media, public and patients.<br>■ Set up a series of Web casts on cartilage repair-related topics and disseminate the schedule to local groups. | ■ Provide a single access point for physicians to streamline communication and referrals.<br>■ Educate referring physicians on emerging surgical technology and techniques to highlight program and surgeon capabilities.<br>■ Ensure 2-way communication: send out personal referral acknowledgment letters and reports within 24 to 48 hours of a new patient exam.<br>■ Recruit primary care sports medicine specialists to address nonoperative cases and improve communication with referring physicians.<br>■ Educate and develop relationships with community orthopedic surgeons. |
| **Third-Party Payers** | **Employers and Sports Programs** |
| ■ Analyze key cartilage repair outcomes and performance factors and communicate the data to payers.<br>■ Develop marketing campaigns targeting regional carriers and case management groups.<br>■ Set up regional on-site payer seminars to educate decision makers on your sports medicine program's capabilities and features.<br>■ Use a physician champion to interact with payers. | ■ Develop a "rapid-response" program for athletes and workers' compensation cases.<br>■ Focus on clinical outcomes, return-to-work/function time and overall cost when discussing contracts for traditional and emerging operative options.<br>■ Develop a regional awareness campaign focused on medium-to-large corporate self-insured employers as well as professional, college and high school athletics programs.<br>■ Collaborate on education programs to identify and integrate at-risk employees into existing rehabilitation programs.<br>■ Collaborate with athletic trainers to cover high school sports programs and recreational leagues and to conduct educational seminars. |

Step #7

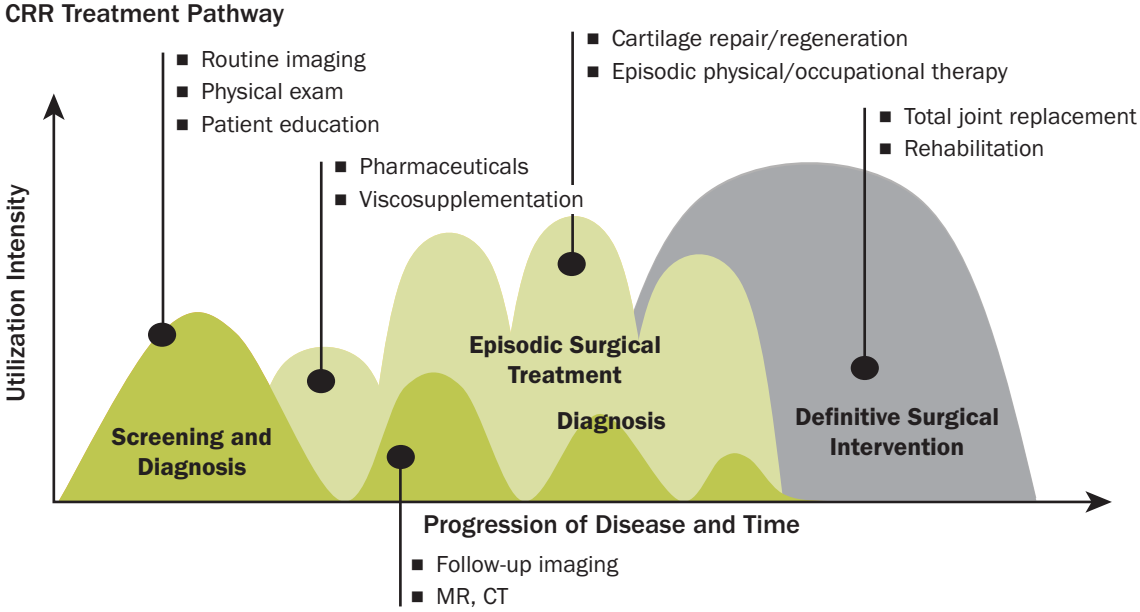
# Capitalize on Upstream and Downstream Interventions

As articular cartilage repair and regenerative medicine emerge as treatment options for younger patients, the number of surgical interventions in a patient's lifetime will increase. Early stage management requires recurring episodes of regenerative intervention, diagnostic monitoring and rehabilitation.

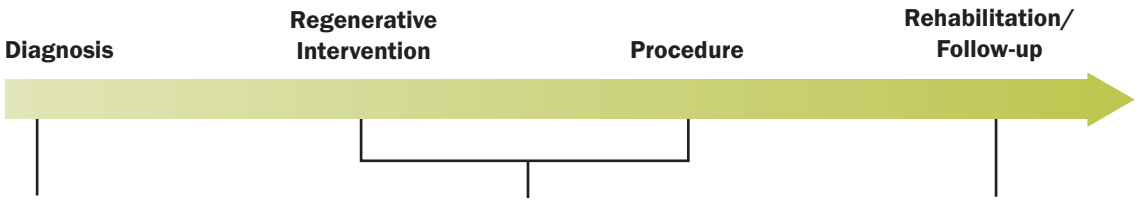
## Episodic Treatment Increases Patient Interactions

Care will assume a cyclical rather than linear progression, requiring integration of emerging techniques into current treatment options and coordination of imaging and rehabilitation care.

**CRR Treatment Pathway**




**Disease Treatment Continuum**




**Increased imaging and diagnostic medicine utilization will drive ancillary volumes.**

- Disease assessed earlier
- Early treatment effectiveness monitored

**Regenerative options will be part of a comprehensive offering.**

- Nonoperative treatments
- Regenerative medicine
- Pain management
- Surgical intervention

**Some rehabilitation revenues will be cannibalized.**

- Earlier intervention to enable incremental growth, reducing need for rehabilitation
- Tailored rehabilitation needed for surgical interventions

CT = computed tomography.

Step #8

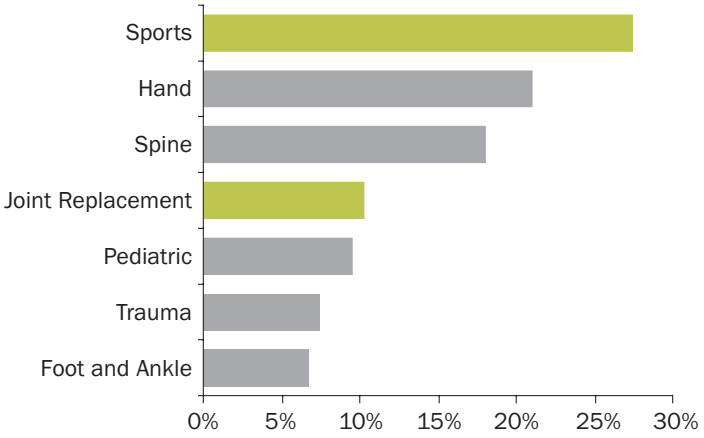
# Collaborate With Select Physicians

Evolving pressures continue to shape the nature of relationships between institutions and physicians. Since CRR is more dependent on technique than on technology, physician collaboration is required to sustain an innovative program and to capture cases as they transition to the outpatient setting.

## Recruit Fellowship-Trained Physicians

Physicians will continue to subspecialize to meet technology demands. Innovation and program differentiation occur when physicians and institutions work together as true partners. Physician integration will become essential to program success, particularly as care becomes more specialized.

**Orthopedic Surgeon Fellowships**
**US Market, 2004**




**Strategies for Recruitment/Retention of Fellowship-Trained Physicians**

- Develop disease-focused services.
- Improve the operational performance of existing services.
- Keep physicians involved in the program's strategic process.
- Initiate long-term succession planning.
- Enhance the physician recruitment process.

## Develop Partnerships With Physicians

Physician partnerships will be required as care becomes more specialized and moves to outpatient disease-specific centers. Common goals that focus on innovative care, quality improvement and efficiency must drive the collaborative process.

- Greater physician involvement correlates to greater success.
- Physicians should drive the redesign of the care-delivery process.
- Hospitals should take a "hands-off" approach to their partners' operations.
- A partnership must evolve from the organization's strategic process, not from a "cookie-cutter" approach. What makes sense for one environment might not apply to another.
- The sports medicine ambulatory surgery center can be integrated with a developed IP program to facilitate translational research and education.
- Relationships must be based on trust and respect. Each party needs to feel that the other is being honest and forthcoming with information and support.
- Timely execution is important to a successful partnership.

# Strategies for Successful Cartilage Repair and Regeneration Programs

CRR technologies are the wave of the future. However, CRR procedures currently have limited success and should be performed only by specialty-trained surgeons. These first-generation technologies require improvements and comprehensive long-term studies and are not appropriate for every institution or surgeon. However, the potential for market differentiation exists for innovators and early adopters who can effectively coordinate patient care by integrating these emerging technologies within the broader menu of surgical options. Moving forward, expect increased payer pressure for evidence-based, cost-effective treatments for cartilage pathology.

| ☑ Strategies for Building a Successful Cartilage Repair and Regeneration Program | |
|---|---|
| **Evaluate Program Capabilities and Strengths** | ☐ Assess institutional core competencies and support needed to successfully implement a CRR offering.<br>☐ Remember that while it is ideal to achieve "organizational competence," all services are not essential in all markets.<br>☐ Integrate total joint replacement and sports medicine programs. |
| **Identify Current Market Offerings and Potential Opportunities** | ☐ Differentiate the program by offering what competitors are not.<br>☐ Assess whether the market size can support the program.<br>☐ Track "medical tourism" developments. |
| **Assess Advantages and Challenges** | ☐ Weigh the competitive advantage for early adopters.<br>☐ Consider the impact of both patient and provider factors in your market. |
| **Evaluate Surgeon and Institution Appetite for Emerging Technology** | ☐ Assess hospital and physician cultural readiness.<br>☐ Evaluate how each technology is integrated into the continuum of care.<br>☐ Ensure that operational and care delivery capabilities support new cartilage repair approaches. |
| **Develop Quality Assurance and Continuous Improvement Matrices** | ☐ Determine what factors are critical to the success of a procedure.<br>☐ Develop outcome measures and share performance data with patients, insurers and referring physicians. |
| **Enhance Stakeholder Communication** | ☐ Provide one access point for physician communication and referrals.<br>☐ Use a physician champion to communicate with payers. |
| **Capitalize on Upstream and Downstream Interventions** | ☐ Prepare for more patient interactions from a rise in ancillary services and surgical procedures. |
| **Collaborate With Select Physicians** | ☐ Recruit fellowship-trained physicians.<br>☐ Partner with physicians and develop common goals for innovative care, quality improvement and efficiency. |

# Appendix: Selected Adult Mesenchymal Stem Cell-Based Cartilage Repair/Regeneration Products

**Selected Adult MSC-Based Cartilage Repair/Regeneration Products**

| Company | Product | Description | Regulatory Status |
|---|---|---|---|
| FIDIA Advanced Biopolymers | TissueTech Autograft System | Hyaluronic acid used to make a scaffold for chondrocytes to grow in cartilage lesions | Launched in 1996, but recently expanded for orthopedic indications |
| Harvest Technologies | Harvest BMAC™ | System to rapidly produce a concentration of mononuclear cells from bone marrow | Studies planned for bone fusion and cartilage repair |
| Mesoblast Ltd/ Angioblast Systems | Mesenchymal Precursor Cell (MPC) Technology | Used to isolate adult mesenchymal precursor cells for bone repair, cartilage regeneration and disc regrowth | Seeking FDA approval for IND applications to orthopedic and cardiovascular conditions |
| Osiris Therapeutics/ Blackstone Medical, Inc. | Chondrogen™ | Injectable, donor MSCs for the repair of meniscal tissue | Enrollment completed for Phase I/II trial for meniscal regeneration and osteoarthritis prevention |
| PrimeGen Biotech, LLC | PrimeCell™, ChondroCell™, OsteoCell™, NervoCell™ | Adult-derived pluripotent stem cells that can differentiate to treat spinal cord injury, rheumatoid arthritis, etc | Proof of concept completed, preclinical trials planned |
| TiGenix | ChondroCelect® | ACI with proprietary molecular markers | Phase III clinical trials for cartilage repair |
| | Adult Stem Cells | Used for cartilage regeneration | Preclinical |
| | ChondroBoost® | Ex vivo stimulation of chondrocytes | Discovery |

IND = investigational new drug application.

## Notes

## Notes

## realize the impact of change

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