Studies on Orthopedic Sports Medicine: New Horizons

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Abstract

Over the last 40 years, orthopedic surgery has been dramatically changed by the adoption of joint replacement, open reduction and internal fixation, and arthroscopy. Concurrently new technologies evolved: biologic concepts aiming to restore damaged tissues and organs using tissue engineering and robotic surgery to improve preoperative and intraoperative planning and to ensure accuracy and precision of the surgery. In this chapter, the current statuses of the two techniques that revolutionize orthopedics are presented.

Abbreviations

ACI	Autologous chondrocyte implantation
ACL	Anterior cruciate ligament
CAOS	Computer-assisted orthopedic surgery
MSCs	Mesenchymal stem/stromal cells
THA	Total hip arthroplasty
TKA	Total knee arthroplasty
UKA	Unicompartmental knee arthroplasty

Introduction

Over the last 40 years, orthopedic surgery has been dramatically changed by the adoption of joint replacement, open reduction and internal fixation, and arthroscopy. Each of these techniques started small but gradually expanded as

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the limitations of the techniques as well as their significant benefits are learned. Robotic surgery is in its infancy in orthopedics. It has found an expanding role in unicompartmental knee surgery, but most other applications remain at only a few centers developing the new techniques.

Concurrent to robotic surgery, "biologic" concepts like tissue engineering, aiming to restore damaged tissues and organs using mesenchymal stem cell therapies, evolved. The current statuses of the two techniques that revolutionize orthopedics are presented.

Mesenchymal Stem/Stromal Cells

The existence of nonhematopoietic stem cells in bone marrow was first suggested by the observations of the German pathologist Cohnheim, 130 years ago. His work raised the possibility that these cells in bone marrow may be the source of fibroblasts and could contribute to wound healing (Prockop 1997).

Friedenstein et al. identified that murine bone marrow contained fibroblast-like colony-forming cells, which differed from the hematopoietic stem cells and generated osteocytes in vitro, providing strong evidence for the self-renewal potential of stem cells (Friedenstein et al. 1976).

Further laboratory studies have confirmed that the cells isolated by Friedenstein can also be found in human bone marrow and could differentiate into a range of different mesenchymal lineage cells including chondrocytes, adipocytes, myoblasts, and osteoblasts. The concept of the mesenchymal stem cell (MSC) has been developed.

Crisan et al. have found that multipotent mesenchymal stem cells exist in many different human organs (Crisan et al. 2008). Studies supporting this fact have shown that MSCs are not confined to the bone marrow and can also be found in the placenta, dental pulp, tendons, skeletal muscle, blood, adipose tissue, skin, trabecular bone, periosteum, synovium, umbilical cord blood, and amniotic fluid (Schmitt et al. 2012).

Stem Cell Definition

Stem cells are defined as unspecialized cells that have the ability to self-renew (proliferation) and potential to form specialized cell types (differentiation) (Schmitt et al. 2012). There are predominantly three classes of stem cells: embryonic stem cells, adult stem cells, and induced pluripotent stem cells (Takahashi and Yamanaka 2006), each with its own advantages and disadvantages.

Embryonic stem cells may only be found in early developmental stages of the organism. They represent the only cell type which possesses the ability to renew itself indefinitely and differentiate into cells of all three germ layers, "totipotent." From a legal and ethical point of view, research involving human embryonic cells is highly controversial and many countries are reviewing their legislation. Moreover, the use of embryonic stem cells is problematic, as the application of allogenic pluripotent cells inheres a distinct oncogenic potential that currently forbids the application in patients (Schmitt et al. 2012).

Induced pluripotent stem cells are a type of pluripotent stem cell artificially derived from a non-pluripotent cell. Takahashi and Yamanaka reprogrammed an adult somatic cell by viral delivery of induction factors or nonintegrating methods and dedifferentiated into a pluripotent embryonic stem cell-like status. The use of induced pluripotent stem cells is also problematic with risk of tumorigenicity and low engraftment efficiency and poor durability (Takahashi and Yamanaka 2006). Adult mesenchymal stem cells are lower in the hierarchy of stem cells and have more limited ability to differentiate into many tissue types, compared to embryonic stem cells and induced pluripotent stem cells. Although the limited differentiation potential of adult mesenchymal stem cells narrows their applicability, this feature provides further advantages like safety for malignant transformation and immune response (Prockop et al. 2010). Adult MSCs present in substantial numbers in many tissues, enabling autologous applications. Decrease in their frequency with advanced age may restrict the autologous applications.

The MSCs of the bone marrow have a greater capacity to differentiate in several tissues when compared with other MSCs of different tissue origin, and the bone marrow aspiration is considered the most useful procedure to acquire MSCs. However, several complications are associated with bone marrow aspiration such as pain, infection, and increased risks of morbidity.

MSCs have the ability to migrate chemotactically to tissues showing inflammation and injury in the organism.

MSCs are known to be powerful immune modulators. They have both immunoevasive and immunosuppressive effects. The injected or naturally released MSCs are activated by the local microenvironment and respond by secreting a site-specific array of bioactive molecules, cytokines. These molecules act to immunomodulate the MSC microenvironment, showing anti-inflammatory activity, and create a regenerative milieu (Kean et al. 2013). Thus, MSCs participate in regeneration by directly differentiating into tissue-specific cells and indirectly influencing tissue regeneration by secretion of soluble factors. Also, they are able to modulate the inflammatory response, promoting vascularization and cell proliferation These features prompted scientists to study the biology of allogeneic MSCs for therapeutic use with appropriate biological and mechanical properties.

Isolation and Expansion of MSCs

MSCs are frequently isolated from the bone marrow aspirate, generally obtained from the superior iliac crest, femur, and tibia. However, since the percentage of putative stem cells in bone marrow MSCs in whole bone marrow is considered as 0.001–0.01 %, an efficient method of isolation is required. This is usually achieved by density gradient centrifugation using Ficoll protocol or Percoll. The cells are layered over Ficoll or Percoll and centrifuged, and the potential MSCs purified.

For clinical application, cell expansion is often needed. Bone marrow MSCs should be appropriately cultured and induced into targeted cells, since their ability to differentiate is easily diminished during culture and passage. The use of ex vivo expansion at MSCs introduces the risk of pathogens and xenoimmunization, due to the usage of fetal bovine serum for culture. In the literature, there is no established and generally accepted cell culture/induction protocol (Kagami et al. 2011).

Application of Stem Cells

Applications of stem cells include four different ways.

The optimal method of application depends on which mechanism of action of the MSC is utilized:

(i) *Application of non-expanded MSCs directly to the site of the lesion*

MSCs can be applied for tissue regeneration without expansion ex vivo in order to avoid cost and time. Typical conventional intraoperative stem cell application is an example. It is simple, easy to utilize whole bone marrow, but lacks a cell concentration strategy and controls their function in vivo.

(ii) *Application of ex vivo-expanded MSCs by systemic infusion*

Studies have shown that MSCs can migrate to the targeted tissue after peripheral injection and remain there for an extended duration. They find their way to the bone marrow by a phenomenon termed “homing.” Chemokines were found to play a key role in homing of stem cells. Systemic infusion of MSCs has been successfully used in treating osteogenesis imperfecta and graft-versus-host disease (Horwitz et al. 2002).

(iii) *Growth on a scaffold and applied directly ex vivo-expanded MSCs to the site of the lesion*

Scaffolds play a critical role in carrying cultured MSCs before implantation and providing a three-dimensional synthetic extracellular matrix environment for tissue regeneration. Studies have shown successful usage of this technique in nonunions and bone grafting.

(iv) *Genetically modified MSCs before being used in a scaffold*

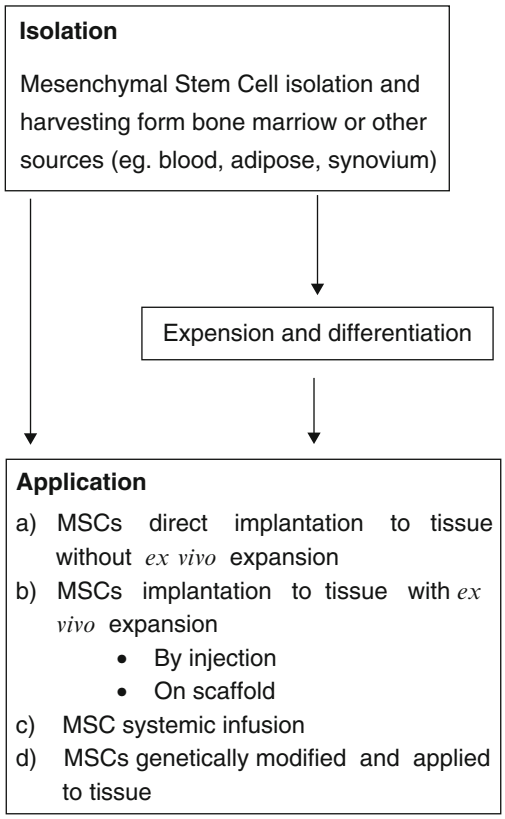

Fig. 1 Diagram showing the process of applying mesenchymal stem cells (MSCs). (1) These are first isolated from the bone marrow or other sources including adipose tissue/blood/synovium. (2) They are either expanded to increase the number or directly applied to the site after centrifugation. (3) After expansion the MSCs are then either applied through a scaffold or injected at the site to aid regeneration

The efficiency of MSCs can be augmented by increasing the expression of growth factors with genetic modification via viral or nonviral vectors. To date, no clinical studies have applied ex vivo-expanded genetically modified MSCs because of the need to identify the optimal growth factor and the vector to ensure effective, safe, and consistent treatment (Kean et al. 2013; Fig. 1).

Cartilage

Articular cartilage is a specialized avascular tissue composed of chondrocytes embedded in a matrix consisting mainly of type II collagen and glycosaminoglycans. Chondral defects of the major weight-bearing joints currently pose an unresolved issue among orthopedists. Cartilage has limited capacity for regeneration because of its limited vascularity. Current treatment methods for osteochondral defects include autograft transplantation, osteochondral allograft, autologous chondrocyte implantation (ACI), and the recruitment of MSC from the subchondral bone to stimulate the formation of cartilage repair tissue by drilling, abrasion, or microfracturing of the subchondral bone (Filardo et al. 2013). Mesenchymal stem cell-based cartilage tissue engineering represents a promising new approach ranging from focal chondral defects to articular OA degeneration. The MSC application techniques were adopted from the clinical experience of autologous chondrocyte transplantation (fibrin, collagen gel, periosteal flap) (Schmitt et al. 2012).

First generation of MSC applications for chondral repair involved direct implantation under a periosteal patch, like early ACI procedures. This technique elicited predominantly good to very good long-term clinical results in the majority of the patients. However, transplant hypertrophy, calcification, delamination, and cell leakage were noted using this technology (Harris et al. 2011).

In second-generation techniques, MSCs were differentiated in vitro within a matrix or bioscaffold and implanted the construct into a chondral defect at cellular maturity. This technique did not follow natural articular cartilage formation pattern. In vitro differentiated and transplanted MSCs may fail to produce articular cartilage or become calcified. For successful outcome of articular cartilage formation, creation of an appropriate in vivo microenvironment is essential. The ideal microenvironment has mechanical stability, to provide appropriate cell-matrix interactions to stimulate tissue growth and capability of functional tissue growth, to protect the cells from axial load and shear forces. It should be highly adhesive to remain stable in the repair site and possesses enough porosity to allow nutrient and differentiation factors to diffuse through it.

Third-generation approach, similar to second-generation ACI techniques, utilizes a bioscaffold seeded with MSCs. Bioscaffolds can reduce cell

leakage and complications from periosteal hypertrophy. MSCs can differentiate and adhere to scaffolds and matrices consisting of synthetic polymers or biomaterials (Filardo et al. 2013).

Intra-articular MSC injections have been investigated for treating chondral defects and knee osteoarthritis. In a recent study, Saw et al. concluded that postoperative intra-articular injection of peripheral blood stem cells in combination with hyaluronic acid after arthroscopic subchondral drilling into grade 3 and 4 chondral lesions resulted in an improvement of the quality of articular cartilage repair over the same treatment without blood stem cells (Saw et al. 2013).

Many aspects in mesenchymal stem cell-based cartilage tissue engineering are still controversial, and they have to be clarified. The optimal MSC source for chondrogenesis and the biological pathways that determine the fate of transplanted MSCs are not yet been identified. MSCs can be isolated from various human sources, such as the adipose tissue, umbilical cord blood, synovial membrane, synovial fluid, periosteum, dermis, trabecular bone, infrapatellar fat pad, and muscle, each presenting various differentiation abilities. The interaction of MSCs with the adjacent osteochondral unit has not yet been explained. The mechanism of controlling the chondrogenesis of MSCs in this milieu is not clarified.

The potential risk considered in MSC use, besides cancer or immunological disease, is differentiation of these cells into unwanted tissue; it implies in theory that the risk of such MSC-mediated endochondral ossification occurs at least in some parts of the repair tissue, thus jeopardizing the formation of good-quality tissue and the clinical outcome (Filardo et al. 2013). The cell-based treatment for cartilage regeneration is still in its infancy and many aspects remain to be explained and optimized. Nonetheless, the cell-based treatment has the potential to be developed in many directions, with different available cell sources, and the possibility to use them concentrated or expand them in vitro, to apply them as a simple minimally invasive injective approach, or to be delivered surgically, alone or augmented with growth factors or scaffolds, and many other improvements are being developed.

Bone

Bone is a dynamic organ, with innate capacity for regeneration and functional restoration upon damage. However, mechanical or metabolic conditions, such as in large defects of bone due to trauma, nonunions, tumor, infection, aseptic loosening, or an inability to heal due to disease or old age, may impair this feature and necessitate augmentation (Steinert et al. 2012). In facilitating bone repair in large defects, bone grafting with autologous bone, the gold standard for bone defect repair, has significant drawbacks, such as limited availability, inadequate quality of graft material, second-site surgery, and donor-site morbidity, leading to prolonged hospitalization. The alternative is the use of donated allogeneic bone. However, allograft lacks the osteoinductive capacities of autograft and has the potential risk of immunogenic alloantigens or pathogen transmission, which limits its use.

Bone tissue engineering has been heralded as an alternative to autografts. The alternative bone graft substitute should reproduce the bone's structural properties combined with the necessary porosity, interconnectivity, bioactivity, and mechanical strength (Steinert et al. 2012).

Successful tissue engineering of bone requires osteoproduction or osteo-competent cell transfer, osteoinduction, osteoconduction, and mechanical stimulation.

Osteoproduction is the ability of the cell to secrete bone material. Healing of critically sized bone defects with purified MSCs derived from bone marrow has been obtained. Osteoconduction relies on the incorporation of a structure bearing bone cells into a recipient site. A structured scaffold maintains space material properties, implants architecture, and provides osteoconduction. Scaffolds must be highly porous with interconnected pores of a diameter of at least 100 μm (ideally between 100 and 400 μm) to allow ingrowth of cells and vessels (Quarto et al. 2001).

Osteoinduction refers to the growth factors that attract osteogenic cells to the site of the defect. In recent years the isolation of factors such as TGF-β3 and its analogues, bone morphogenetic proteins (BMPs), BMP-2 and BMP-7, has led to their use clinically to enhance and accelerate the

repair of bone and also to replace it. Mechanical stimulation and other biophysical stimuli appear to be critical factors for the proliferation and differentiation of bone cells and for the formation of both bone mineral and structure.

The clinical use of culture-expanded osteoprogenitor cells in conjunction with porous hydroxyapatite scaffolds has been reported in treatment of four patients with diaphyseal segmental defects. The defects ranged from 3.0 to 28.3 cm three in a tibia, a humerus, and two separate ulnar fractures. As a result, there was progressive integration of the implants with the surrounding bone, progressive new bone formation inside the bioceramic pores, and vascular ingrowth. No major adverse reactions were observed. Radiology evaluation showed that bone formation was far more prominent over the external surface and within the inner canal of the implants (Marcacci et al. 2007).

Nevertheless, tissue-engineered bones have delivered less than optimum results because they appear to be more sensitive to adverse environments of the host soft tissue site, such as marginalized vascularity, and provide a mechanical construct environment, important for favorable bone formation.

Tendon

Tendon injuries are being increasingly seen as people are more physically active and also turn older. Tendons may not only be harmed by acute trauma but also substantially weakened with the effect of chronic inflammatory insults during enduring tendonitis, tendinosis, bursitis, or epicondylitis and eventually resulting in tendon rupture. The most frequently affected tendons are the supraspinatus tendon of the rotator cuff, the Achilles tendon, flexor tendons of the hand, as well as the anterior cruciate and medial collateral ligaments of the knee

The repair of damaged tendon tissue is a complicated process, requiring a lot of time to regain biomechanical levels. Current treatment options are implanting autografts, allografts, and synthetic prostheses. Possible side effects of surgical treatment with autografts are nerve damage, donor-site morbidity, muscle atrophy, stiffness, scar formation, and decreased mobility (Longo et al. 2011).

Experience in the preparation and use of allogeneic grafts for tissue regeneration has shown that the micro-architecture is quite dense and residual cells at small amounts may remain. These grafts initiate prolonged inflammatory responses in vivo and require longer times to incorporate into native tissue and remodel (Longo et al. 2011).

Current tissue-engineering strategies have relied predominantly upon scaffolds derived from both synthetic (polyglycolic acid) and naturally derived (collagen) materials to form the cell-scaffold construct. The breakdown products of synthetic scaffolds are known to be antimitotic and cytotoxic in vivo. Most scaffolds, both synthetic and naturally derived, are deficient in the initial mechanical strength to permit immediate motion and rehabilitation after implantation, which lead to subsequent adhesion formation, decreased range of motion, and poor functional outcomes (Whitlock et al. 2007).

Vastly emerging MSC-based applications are considered as a trend option for tendon regeneration and presently being studied in humans, rabbits, rats, and horses. MSCs might be used to create a “neoligament” with the prerequisites of a suitable cell source, a biocompatible scaffold, and a biomechanical environment that promotes safe healing and organized maturation (Petrigliano et al. 2006).

An ideal scaffold for tendon and ligament regeneration would be (1) naturally derived from either allogeneic or xenogeneic material amenable to host-cell-mediated remodeling in vivo; (2) devoid of cellular material to minimize inflammatory potential, disease transmission, and host immune response; (3) cytocompatible; (4) of optimal micro-architecture to promote efficient cell seeding, infiltration, and attachment of the recipient’s own cells prior to or after implantation; and (5) distinguished by sufficient biomechanical integrity to withstand rehabilitation until complete remodeling has occurred.

The studies on Achilles repair in rabbits have shown that implantation of bone marrow-derived MSCs within a fibrin vehicle to the tendon or injection of MSCs at the site of Achilles reinsertion to the bone improved the morphologic

and biomechanical characteristics of Achilles. Bone marrow-derived MSCs have improved the healing of tendonitis lesions in the equine collagenase model (Schnabel et al. 2009).

Clinical application of cultured bone marrow-derived MSCs in clinical tendonitis in racehorses has also resulted in improved return to athletic activity in long-term studies (Godwin et al. 2012).

In rat studies, rats with surgically created partial ACL lesions treated with intra-articular stem cell injections to accelerate ACL healing presented superior histological scores and withstood greater mechanical resistance, compared with the control group (Longo et al. 2011).

Intraoperative bone marrow MSC application to the proximal humerus anchor holes during arthroscopic rotator cuff surgery demonstrated improved outcome compared with previous experiences with suture repair alone (Ellera et al. 2012).

There have been no commonly accepted standardized protocols for differentiation of MSCs into tenocytes. Differentiation of stem cells into the correct cell types necessitates to be linked with a molecular signaling molecule. The mechanism of molecular signaling guides the stem cell in tissue regeneration, maintenance, and repair (Ahmad et al. 2012).

Meniscus

The meniscus is a fibrocartilage structure in the knee joint functioning to increase surface contact area, absorb mechanical loads, and improve stability, lubrication, and proprioception (Osawa et al. 2013). Injury or removal of the meniscus alters the loading environment in the knee joint, predisposing an accelerated onset of degenerative joint changes, articular cartilage degeneration, and osteoarthritis. Treatment options include partial meniscectomy, meniscus repair with fibrin clot, meniscus repair, fibrin sealant, laser welding, and meniscal allograft transplantation. However, all these techniques mentioned are limited in that they are only effective if a tear is within the vascular region of the meniscus.

Mesenchymal stem cells represent a potential dual role for meniscus repair, both by differentiating into fibrochondrocytes and producing special growth factors for its repair. The search for the optimal source of mesenchymal stem cells for meniscal regenerative potential was obtained from synovium and bone marrow (Horie et al. 2012).

Synovial mesenchymal stem cells can be harvested minimally invasively, from synovial tissue, and easily expanded in culture. Multiple studies suggested that synovial mesenchymal stem cells possess a particularly high capacity for chondrogenic differentiation and proliferation compared with mesenchymal stem cells obtained from other tissues, such as bone marrow or periosteum. They are also capable of adhering to damaged intra-articular structures such as the meniscus and participating in the repair process in rat models. The mechanism of integration may depend on interplay of the stem cells with surrounding meniscal tissue in response to chemotactic signals (Horie et al. 2012).

The ability of synovial mesenchymal stem cells to adhere independently to the site of meniscal injury, differentiate into fibrochondrocytes, and synthesize a new matrix that closely resembles native meniscal fibrocartilage without a scaffold or extrinsic cytokines seems to negate the need for such additional stimulus. Moreover, this approach avoids the potential for complications associated with disease transmission and immune reaction. It is also possible to use synovial mesenchymal stem cells in combination with a tissue scaffold for large meniscal defects in patients with little inherent regenerative capacity (Horie et al. 2012).

Investigators have demonstrated improved healing rates in meniscal tears supplemented with synovial flaps or grafts in animal models (Jitsuiki et al. 1994) and synovial rasping in human clinical studies (Shelbourne and Rask 2001; Uchio et al. 2003).

Computer-Assisted Orthopedic Surgery

Computer-assisted orthopedic surgery (CAOS) is defined as the use of computers and robotic technology to assist the orthopedist in providing musculoskeletal care, in which machine capability of precision and accuracy is coupled with human

judgment and skills to perform a task better than either could do alone (Specht and Koval 2001–2002).

The CAOS principle is preoperative planning, intraoperative navigation, and smart remote surgical technologies. The orthopedic surgeon's judgment, experience, adaptability, and knowledge are augmented with computer characteristics of "geometric precision, reproducibility, perfect 'memory,' lack of fatigue, and insensitivity to radiation."

Preoperative planning includes a digital image formation which serves as a map to guide through the operation for each particular procedure. Surgical instruments can be integrated into the map so that their position, attitude, and progress can be controlled and monitored to an accuracy of fractions of a millimeter or degree (Sikorski and Chauhan 2003).

The systems used for producing the digital maps are subdivided into three categories:

"Preoperatively imaged system" requires anatomical information which is collected before operation in the form of a CT scan or MRI.

"Preoperatively imaged" in which anatomical imaging occurs in the operating suite at the time of surgery. Usage of a specially modified fluoroscopy unit is needed. Maneuvering is required during surgery, with probable consequence of time loss and potential for infection. The data are transferred directly to the computer through a hardwired connection. The data are transferred directly to the computer through a hardwired connection. These two groups comprise the "image-based systems." They usually need considerable preoperative planning as well as the acquisition of the images.

The third category is "image-free," in which an anatomical model is embedded in the software and is upgraded by the process of registration.

All systems include "registration." Registration is the process of matching two coordinate systems into spatial alignment. The accuracy of the registration process is fundamentally important. Although averaging algorithms are used, a poorly performed registration will result in decline of the accuracy of the alignment.

After specifying the location of landmarks of each bone using a pointer, the computer can track the position of markers, cut surfaces, and axial alignment. Tracking devices, also known as localizers, are used to track the positions of instruments relative to patient anatomy (Cleary and Peters 2010). The computer screen acts first as an interactive data-gathering instrument and later provides the visual images necessary for the surgery. Today, the acquisition of three-dimensional data (3D rendering) from medical imaging modalities is the norm rather than the exception. The physician uses this virtual display to manipulate the instruments to accomplish the procedure. A confirming image is obtained upon procedure completion.

As a critical component of computer-assisted surgical applications, the software constructs the structural model, integrating and correlating the data from tracking systems, and displays real-time updates of the instruments and patient.

Applications

Pedicle-Screw Insertion

Historically, this was one the first areas for CAOS. The surgical outcomes such as neurological complications and health outcome scores are usually correlated with the screw insertion accuracy (Tian et al. 2011). The placement of a pedicle screw requires precision to align the screw along the pedicle of the vertebral body and to avoid complications. Merloz et al. were among the early pioneers in this area, who evaluated navigation assistance for screw placement in the thoracic and lumbar spine with good results (Merloz et al. 1998). The systematic reviews and meta-analysis of comparative studies have shown that navigation compared to conventional methods provided a higher accuracy in the placement of pedicle screws. The superiority of navigation systems was obvious when they were applied to deformed spinal structure (Tian et al. 2011).

Kantelhardt et al. demonstrated that robotic-guided pedicle-screw placement accuracy was

higher than conventional screw placement. Duration of intraoperative radiation, postoperative administration of analgesics, and duration of postoperative hospitalization and rates of adverse events were significantly lower in robotic-guided compared to conventional procedures (Kantelhardt et al. 2011).

Total Hip Arthroplasty

Total hip arthroplasty (THA) is considered to be one of the most common and successfully performed orthopedic interventions. The position of the acetabular component is critical to the function and outcome of THA by improving longevity and decreasing the dislocation rate (Gurgel et al. 2013). Being introduced as THA in 1998, it was one of the earliest procedures to which computer-assisted systems were applied. The doubts that persist about navigation in general are its real benefit, its cost, the longer surgical time, and the potential complications.

In their study, Gurgel et al. have concluded that computer-assisted THA is a safe and reproducible technique that increases surgical time very little and does not present any specific complications due to the method and that computer-assisted surgery improves our technique and has to be more developed (Gurgel et al. 2013). Manzotti has found similar clinical outcomes of computer-assisted THA compared to conventional methods and stated that using computer navigation in THA could enhance the surgeon's ability to correct limb length discrepancy (Manzotti et al. 2011).

Knee Arthroplasty

Knee arthroplasty, especially total knee arthroplasty (TKA), is another common orthopedic intervention that has been established as a reliable and cost-effective treatment to alleviate pain and restore physical function in patients with severe knee arthritis. Malpositioning of the implant can lead to early wear and loosening, as well as inferior functional performance, and thus reduces implant longevity (Cheng et al. 2012a, b).

Achieving reliable alignment of the components in unicompartmental knee arthroplasty (UKA) using conventional approaches is difficult on a consistent basis. Computer navigation was introduced to improve the positioning based on the patient's individual anatomy and increase the accuracy of UKA. Navigation systems have been shown to reduce the number of alignment outliers resulted from conventional instruments (Netravali et al. 2013). The development and introduction of minimally invasive surgical techniques had the potential to compromise implant alignment accuracy by decreasing the sight during operation (Argenson and Flecher 2004). Robotic assistance refined and enhanced the improvements seen with computer navigation in increasing the accuracy of bone preparation techniques (Dunbar et al. 2012).

A recent meta-analysis concluded that CAOS has improved the accuracy of the coronal alignment of the lower limb and implant, which are a common factor in early failures following TKAs (Cheng et al. 2012a).

Trauma Surgery

Computer-assisted trauma surgery allows navigation of surgical instruments relative to patient anatomy in an improved visual environment. Complex invasive procedures can often be performed using minimally invasive techniques, which lead to less tissue damage with improved wound healing. The main imaging modalities used with computer navigation in orthopedic trauma are fluoroscopy, CT, and 3D fluoroscopy. Of these, fluoroscopic and 3D fluoroscopy-based navigations allow acquisition of real-time data and therefore used more commonly.

The most commonly used applications of computer-assisted trauma surgery are in reduction and the alignment of fracture, IM nailing, percutaneous cannulated screw fixation and plating, and hardware or shrapnel removal. Proposed benefits are increased accuracy, minimized invasiveness, and less radiation exposure. Current drawbacks include increased surgical time, equipment handling, and cost (Atesok and Schemitsch 2010).

Tumor Surgery

Computer-assisted tumor surgery offers several potential benefits in the surgical management of patients with musculoskeletal tumors. It may facilitate location for resection and reconstructions in patient's inadequate resection margins

are associated with higher risk of local tumor recurrence and poorer patient survival (Picci et al. 1994). The real extent of tumor in the bone may be determined with the advent of effective chemotherapy and accurate MRI (Gillespy et al. 1988), and it may allow a joint-preserving tumor resection (Wong and Kumta 2013). One study has reported that the surgical accuracy of an experienced surgeon in performing a pelvic tumor resection with planned 1-cm surgical margins (±5 mm) with a probability of only 52 % (Cartiaux et al. 2008). Preoperatively, computer-assisted tumor surgery provides improved visualization of the operative field and facilitates surgical planning. Intraoperatively, real-time data of imaging can be merged with MRI and CT scans to create a virtual map of the operative field. It may facilitate improved accuracy and superior precision in excision of bone tumor and may enable an accurate reconstruction to be performed (Cheong and Letson 2011). Both improved accuracy and superior precision in excision of tumor have been beneficial for patients, particularly with regard to implant positioning and function. Computer-assisted tumor surgery may facilitate the precise resection of the bone tumor and may enable an accurate reconstruction to be performed (Wong and Kumta 2013).

Anterior Cruciate Ligament Surgery

Anterior cruciate ligament (ACL) rupture is one of the most common sports injuries in active young people. ACL rupture is commonly treated with surgical reconstruction to allow patients to return to an active lifestyle (Cheng et al. 2012b). Two common mechanisms of graft failure include impingement along the intercondylar notch and anisometry. Anisometry is a term used to describe the phenomenon in which the distance between the tibial and femoral tunnels changes with flexion and extension of the knee (Cheng et al. 2011). The correct tunnel placement is one of the crucial factors for the success of ACL reconstruction. Conventional techniques can still result in high variability in tunnel location. Computer-assisted navigation systems are designed to improve accuracy and consistency of femoral and tibial tunnel positioning and efficiently restore knee kinematics, taking into consideration anatomic references and final graft isometry (Kodali et al. 2008; Zaffagnini et al. 2010).

Randomized, controlled trials have revealed that that the computer-assisted group had improved measures of laxity and other alignment variables, but no statistically significant improvements in functional outcomes (Plaweski et al. 2006; Mauch et al. 2007; Hart et al. 2008; Chouteau et al. 2008).

The computer-assisted navigation systems for ACL reconstruction have increased concerns regarding the learning curve, higher costs, and time-consuming problems. Based on these factors, there are still major difficulties to the routine use of computer-assisted navigation systems for ACL reconstruction in clinical practice.

Computer-assisted orthopedic surgery is making an impact in many areas of practice. Today the main concerns about CAOS are cost and time. The use of CAOS in sports medicine results in improved preoperative and intraoperative planning and finally more precise surgery. With continued improvement in technology and techniques, registration will improve the accuracy and the speed of the procedure, leading to more precise surgery with less surgical time. Also, the costs will reduce as the costs of computing and navigation technology decrease with the expanded use of CAOS to multiple surgical techniques with a higher utilization and more rapid amortization.

Conclusion

Over the last 40 years, two concurrent but different concepts in orthopedics have been developed based on technological developments: robotic surgery and tissue engineering with mesenchymal stem cells.

Robotic surgery enables safe and accurate surgery in joint replacement, open reduction and internal fixation, and arthroscopy, with its characteristics of “geometric precision, reproducibility, perfect memory, lack of fatigue, and insensitivity to radiation.” Virtual reality in robotic surgery assists training in complex procedures in

orthopedics. Currently, the main disadvantages are cost and time consumption, which is thought to disappear as technology evolves.

Application of mesenchymal stem cells in orthopedics is in its infancy. Still there are risks of tumorigenicity and low engraftment efficiency and poor durability. To achieve full therapeutic potential of stem cells, further research about native stem cell function and pathways is needed. The clinical application of mesenchymal stem cells is a promising "biologic" concept to regenerate musculoskeletal system after interdisciplinary researches.

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