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The Future of Orthopedic Medicine

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The Future of Orthopedic Medicine

WMU Lee Honors College Thesis

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Abstract

Orthopedic medicine is changing and advancing along with the rest of the medical field. There are new concepts developing in orthopedic trauma, tissue engineering, collagen, nano-orthopedics, biodegradable implants, robot-assisted surgery and more. The changes to orthopedics are focused on the changing needs of patients, and orthopedists are also changing their ways to keep up with the demand required of them. Advancements in fields such as stem cells, imaging technology, functional tissue engineering, and robotic assistance will further propel the diagnostic and treatment abilities of orthopedic medicine. In order to accomplish these advancements and provide for the needs of the future patient, more research will be required as it is the key to the future of orthopedic medicine.

Orthopedic Medicine, along with the rest of the medical field, is changing at a rapid pace. Technology is modifying the ways medicine is practiced, providing more efficient treatment options along with decreases in medical errors. Continued advancements in medicine and technology will lead us to a day when a holographic scan of our entire body can be projected in an office and surgeons can perform surgery through computers all over the world.[15] This would help provide better diagnosis, treatment options, and recovery monitoring for all types of orthopedic procedures. Many developments in tissue and implant engineering are being developed that will soon replace the current less functional options. The orthopedic patient is changing as our population continues to age, thus less invasive surgeries with faster recovery times will be required to provide a continued quality of life. The role of orthopedists is changing as well as an initiative for increased participation in research is growing. The movement for further research participation and funding is imperative, as it is the only way to discover the future of orthopedic medicine.

The Future Patient

The future of orthopedic medicine hinges on the future patient and what requirements they will have of the field. We've been aware of the looming situation; baby boomers are aging and life expectancies are growing so that means a great deal of orthopedic medicine's resources are placed on the aging patient. The aging population certainly has many medical needs, and their orthopedic needs, ranging from musculoskeletal injuries, osteoarthritis, and osteoporosis, are plentiful. Their lack of mobility, decrease in strength of muscles, tendons, and ligaments, and extensive wear on their bodies can lead to a great deal of issues and injuries. The mechanical properties of tendons and ligaments diminish with age which was shown in a study of the ACL which was measured to be 1.3 to 3.3 times stronger in subjects 22-41 years of age than subjects over 60.[15] Unfortunately, few studies or preventative measures have been made to look for ways to avoid or delay issues faced by the elderly. The Bone and Joint Decade coalition has been promoting partnerships to raise awareness, but a specialized society to push for more attention and awareness to the elderly would be a better solution.[7]

Arthritis is the most popular reason for an orthopedic consult, and it has a large impact on the quality of life for the individuals it affects. A new technique for diagnosing and tracking progression of osteoarthritis being developed involves tracking Biomarkers. Biomarkers of osteoarthritis are the products of cartilage breakdown, such as the molecule aggrecan, and metabolic byproducts of chondrocytes which can be effective signalers of the progression and severity of the disease.[11] This technique could allow for earlier and more precise diagnosis of osteoarthritis and would help to choose the most effective and appropriate medicine or surgery required at their stage of progression. A few properties of biomarkers requires further research such as the change of presence with and without treatment, how abundant the biomarkers are if only one joint has arthritis, and if blood, urine or synovial fluid is best route of measurement based on the metabolic pathways followed by the biomarkers.[11] A better understanding of the process specificity of different molecules and enzymes will lead to better treatment and diagnosis between different types of arthritis.

Another issue faced by the aging patient and especially women is osteoporosis, which affects an estimated ten million Americans.[11] More effective and quick routes of identification of osteoporosis require a better understanding of the disease and more advanced imaging than current bone mineral density scans. Some new technologies are being developed to provide a more accurate picture of the molecular structure of a patient's bone tissue and are called Fourier transform infrared spectroscopy and solid-state nuclear MRI. The spectroscope can measure the mineral amount and arrangement while the MRI can measure the mass of hydroxyapatite in the bone.[11] The two together can provide a more complete indication of the current risk of fracture faced by the patient.

The aging patient has many medical ailments to be concerned about, and musculoskeletal injury is certainly one of them. Serious enough injuries can lead to a bed ridden end to their lives because the very invasive surgeries they might require would be too big of a risk. An effort towards more minimally invasive surgeries and quicker recovery times are vital to avoid tragedies such as these.[3] Better and smaller medical technology and smarter surgical techniques will answer this need. Patients will also expect their extended life expectancy to remain comfortable, so any chronic injuries brought upon by their previously active lifestyle will have to be treatable into their old age.[3] Without progression in orthopedic medicine, living longer lives will also mean more pain and less mobility.

Innovative Concepts in Orthopedic Trauma

There have been several innovative concepts developing recently in orthopedic trauma involving new surgery techniques that are still being studied in hopes of easier surgeries and improved recovery. One such development is a partial combination of two current techniques; intramedullary nailing and distraction osteogenesis. The new concept itself is called distraction osteogenesis over intramedullary nailing and includes four possible techniques including lengthening over an intramedullary nail, lengthening followed by intramedullary nailing, lengthening combined with plating, or the use of internal lengthening devices.[12] The purpose of these techniques is to stretch the bone and allow growth to reoccur with the use of intramedullary nails or plating to help stabilize the weak growing section of bone. Intramedullary devices are being included in these techniques because biomechanical studies have shown their benefits of a shortened lever arm during joint movement, increased load sharing, and the ability to be inserted through small incisions.[14] These new methods have been shown to decrease the external fixation needs, protect from bone refracture, and provide a faster rehabilitation time, though they also are surgeries that are more susceptible to infection, more blood loss, longer, and thus, more expensive surgeries so more research is needed to make the techniques as beneficial as possible.[12]

Another innovative concept in orthopedic trauma specifically important to fractures in the aging population is Percutaneous Pelvic and Acetabulum Fixation. Pelvic and acetabular fractures are becoming increasingly common in our aging population and hip replacement surgery is usually too invasive of a surgery for them to endure. To avoid this, percutaneous reduction and fixation techniques used on other parts of the body are being adapted for use on the pelvis and acetabulum. These techniques usually involve the use of pins through the skin to reduce fractures and hold them in position so healing can take place. Percutaneous pinning is becoming more popular because it minimizes soft tissue injury and surgical morbidity that occurs from surgeries like joint replacements.[14] The benefits of Percutaneous Pelvic and Acetabular Fixation include reduced surgical time, blood loss, and stress to the patient frequently seen after joint replacement due to the extensive rehabilitation period. The negative effects include possible hip instability and post-traumatic osteoarthritis which isn't addressed like it is during a joint replacement.[8] Further research is needed to the benefits of this repair to such complex fractures are great enough.

A final innovative concept in orthopedic trauma, which is another advancement of a current technique, is called Inflatable Intramedullary Nailing. This new technique, available specifically to long bones, is exactly how it sounds, a nail that inflates inside the medullary canal adding pressure to the canal walls leading to greater friction between the surfaces. As a result of the increased pressure, there is an increase in torsion and bending resistance in the bone up to four times greater than current IM nailing techniques. Since the hydraulic inflatable nail is implanted in its unexpanded form, it is much easier to implant resulting in less surgical time and fewer reoperations compared to current IM nailing.[4] Also, since the interface between the intramedullary nail and the bone tissue is much different and tighter, there is expected to be an increased fracture stability and biocompatibility between the two surfaces.

These new techniques are all being studied to provide an increased load sharing and healing rate along with decreased surgical time and invasiveness of body tissues. They also look to increase patient mobilization and weight-bearing ability which results in shorter hospital stays and medical costs.[14] Further study and discovery of other techniques will continue this trend and result in better clinical and functional outcomes.

Engineering Tissue Interfaces

Tissue engineering is a fairly new field in orthopedic medicine, and new challenges and concepts to research continue to develop from it. One such concept being looked at today is the tissue interface, or the area where one structural tissue transitions into another. This area of tissue plays a vital role in transitioning mechanical load between connected tissues. So not only do individual orthopedic tissues need to be regenerated, but also the biochemical and cellular layout of the interface linking different tissues types together must be matched and regenerated.[17]

One very important tissue interface with regard to our aging society is the cartilage-bone interface because it is the primary site of osteoarthritis, which affected 27 million people in the United States alone in 2008.[17] Regeneration of cartilage tissue is an important topic of research because since it is not a very vascular area, the body isn't able to repair cartilage on its own very well. The challenges and goals faced by those engineering osteochondral tissue is to develop a very low friction surface to be used at an articulation site and for the material to integrate and maintain the same mechanical properties as the cartilage and bone that is implanted.[17] Four different approaches are being taken towards osteochondral scaffolds: a scaffold design for the bone and no scaffold for the cartilage, separate bone and cartilage scaffolds that are combined during implantation, a heterogeneous composite scaffold of the two, and a homogenous scaffold of the two.[17] Scaffolds are split into two types; hydroxyapatite (HA), or synthetic, and natural polymers. Hydroxyapatite scaffolds offer great strength and bone integration but can result in cartilage irregularities while synthetic and natural polymers are a bit weaker yet allow for much more adaptable geometries and fits. After a scaffold type is chosen, it is loaded with cells of osteogenic and chondrogenic properties to elicit regeneration of tissue after implantation.[17] An example of this was done in a study that created replacement vertebral discs by seeding cells taken from the nucleus pulposus and annulus fibrosus from a healthy vertebral disc into a synthetic scaffold and allowing the tissue to grow.[11] Proper implantation and integration between the new osteochondral scaffold and the existing tissue is imperative in order to avoid future instability or failure of the articular surface. The future outlook of osteochondral interface tissue engineering is to ensure integration with existing cartilage, adjusting scaffold stiffness and degradation rate to that of the regenerating tissue, and replicate the properties and structure of the calcified cartilage zone at the tissue interface.[17]

Another important tissue interface is the tendon or ligament and bone connection site because that is affected during many injuries such as sprains. Current works have focused on improving the graft anchorage when re-attachment of the tendon or ligament to the bone is required. An example study using the ACL showed the use of bone morphogenic protein-2 as a potential stimulant for the formation of a natural insertion of the ACL into bone.[15] In tendon/ligament tissue engineering, the most widely used scaffold types are silk, collagen, and poly-L-lactic synthetics which are combined with cell sources such as stem cells or fibroblasts and other growth factors to initiate extracellular matrix production. [17] The silk scaffolds have proved to be advantageous because of its ability to be woven into rope-like braids and made to match the stiffness of tendons and ligaments without loss of strength. This braiding technology can also be used with poly-L-lactic synthetics and allows for control of mechanical properties, pore sizes, which can be more porous near articulation areas and less porous near attachment sites, degradation rate, and similar geometry. [17] Research is also being done on ways to recreate the interface between existing grafts and bone, which is especially beneficial after tendon reconstruction. Other work is focused solely on synthetic materials with no cell addition, which instead stimulate cell migration towards the scaffold and eventually new bone formation.[17] The future challenges of ligament/tendon-bone interfaces include creation of an optimal scaffold, cell source, and extracellular stimulus to recreate fibrocartilaginous tissue, which can form the interface between the tendon/ligament and bone. This could be solved either by the linking of two separate mixtures which connect to their specific structure type or through the creation of a composite mixture that gradually transitions from tendon/ligament tissue to bone tissue. Further knowledge gain in this arena will lead towards the generation of whole tissue units which could be implanted instead of current graft transplants.[17]

While little work has been done at the meniscus-bone interface site, it is an important area, especially to sports medicine, that will likely see greater research in the near future. When menisci tissue becomes damaged, a portion often needs to be removed which can lead to an early onset of osteoarthritis. Thus, studies are being done with both natural and synthetic polymers for meniscus tissue engineering scaffolds. One currently under clinical phase-II trials is a non-cellular collagen based implant.[17] Another non-cellular scaffold is made of a gelatin hydrogel and is loaded with platelet rich plasma which, during trials, resulted in increased tissue integration and fibrochondrocyte cell aggregation in comparison to older scaffolds. One final matrix type that has been studied is an enzymatically processed grafted meniscus tissue. Those scaffolds, which were seeded with cells, resulted in a greater fibrocartilaginous tissue response and also a greater cross sectional area.[17] Issues that must be solved with future research in this area include discovering the ideal cell source and growth factors for developing meniscus tissue that is mechanically stable and deposit extracellular matrix, and also gaining a greater understanding of the meniscus-bone interface, which is imperative to the success of graft fixation. Creation of a fibrocartilaginous transition area and an integrated tissue unit will also be an area of research. And while research isn't currently focused on the meniscus-bone interface, there are many similarities between it and the tendon/ligament-bone interface, so advancements in that area will likely also be beneficial to the meniscus-bone interface.[17]

The final orthopedic tissue interface is the muscle-tendon interface, or myotendinous junction. This junction site is the most common site for injuries to muscular tissue. This is another tissue area that has not received a great deal of attention, but further investigation could result is future muscle tissue engineering possibly creating entire muscle tissue units.[17] The drug Suramin was found to increase muscle healing and function after injection at an injury site.[11] Another study using rat Achilles tendon fibroblasts and soleus muscle myoblasts cultured the two tissues separately, then pinned the two tissues together and allowed to co-culture and eventually formed a muscle-tendon interface. Much more work remains in this type of interface engineering and some main issues are still present. One very important issue is the inability of the engineered muscle tissue to generate as great a force as the original muscle it is connecting with. Also, as the engineering size increases, the issue of increased vascularization arises which will impede growth. Finally, the interface between the muscle and tendon must be very efficient and provide a proper load transfer to bone or can otherwise result in tissue failure.[17]

These four tissue interfaces are each structurally vital to our muscles and joints, but each has a large amount of research yet to be done. The goal of engineering each one is to provide a smooth transition between the tissues of differing mechanical properties to reduce the risk of tissue failure. A better knowledge of the developmental biology of the interface sites will assist in their creation. New techniques of interface tissue characterization and simultaneous culturing of the required cell types must be discovered. Lastly, outcome measurements needs to be established to assess the structure and biocompatibility of the interface to ensure proper load transfer and eliminate the risk of mechanical failure.[17] Research demand in this field is high but will continue to open new doors in orthopedic medicine.

Collagen Scaffolds for Regenerative Medicine

We take a deeper look now at the molecular structuring of scaffolds in regenerative medicine/engineering specifically with collagen based materials. Scaffolding is a great technique used for tissue regeneration because it provides the porous three-dimensional template for growth and can be seeded with growth cells or loaded with bioactive molecules to facilitate repair or extracellular matrix production. Collagen based scaffolds have great advantages with use as biomaterials in regenerative medicine. Its mechanical properties can be a potential issue, though it can be overcome when cross-linking techniques are used or when made into a composite with substances such as hydroxyapatite.[6] The general goal of tissue engineering is to assist with the growth of new yet naturally functioning tissue. In bone tissue engineering for example, the scaffold must possess both osteoconductive and osteoinductive properties. In other words, the scaffold should support the deposit of new tissue while also possessing inherent signals which stimulate tissue regeneration.[6] The collagen scaffolding should also have a porosity of >90% to allow nutrients to diffuse before implantation and for vascularization to permeate after. Degradation of the scaffold should also occur at a rate as close to the regenerative rate of the tissue as possible.[6]

The ease of biocompatibility with collagen comes from the fact that it is the most abundant protein in the human body. This and its biodegradability and hydrophilic characteristics have lead to its use in research involving tissue engineering in tendon, dermal, neural, brain, adipose, dental, and cartilage tissue.[6] Soft tissues especially have shown promising results though bone and cartilaginous tissues require further research due to the high load bearing characteristics they have. Collagen has a specific helical structure, which is very important in protecting the protein from being broken down by protein enzymes called proteases and also allows for strong cell adhesion and assembly of extra-cellular matrix. Its strong properties make collagen an ideal candidate for manufacturing tissue-engineered scaffolds in many different ways including rapid prototyping techniques, critical point drying, electrospinning, and freeze-drying. The relatively poor mechanical properties of collagen scaffolds compared to the natural tissue it replaces can be overcome either by crosslinking treatments or through combination with a stiffer, reinforcing material forming a composite.[6] The purpose of crosslinking treatments is to strengthen and stabilize the bonds between the three helices of the collagen fiber and also the bonds between separate molecules of collagen. There are chemical methods of crosslinking including the use of glutaraldehyde carbodiimides, and there are biophysical methods including the use of ultraviolet light and dehydrothermal crosslinking.[6]

Recent opinions have moved towards developing collagen composite materials, which have adequate mechanical strength and also the necessary porosity and degradation abilities. This is because collagen has been shown great results when combined with other materials such as synthetic polymers, organic molecules, and calcium phosphate ceramics. Synthetic polymers provide a strong three dimensional structure while the addition of collagen provides the necessary biocompatibility of the scaffold, organic molecules add the ability of manipulation of cellular behavior, and calcium phosphate reinforced the collagen structure while also inducing osteoinductive properties.[6] The biomaterials, which are chosen to be combined with collagen, can be optimized for the setting they are used in. For example, when glycosaminoglycans (GAGs) are used in combination with orthopedic scaffolding, results have shown the scaffold to have chondrogenic and osteogenic properties. GAG incorporated collagen scaffolds have also shown an increase in cell growth and movement through the scaffold in bone, cartilage, and tendon experiments.

The combination of collagen with ceramics, such as calcium phosphates and bioglass, has shown to greatly reinforce the collagen while promoting bioactivity. The bioglass adds stiffness and compressive strength to the collagen while calcium phosphates, such as hydroxyapatite, promote osteogenesis within the scaffold. Multiple studies have shown this improved strength, healing and osteogenic ability with the addition of hydroxyapatite, even one using stem cells which found the composite to positively influence the osteogenic differentiation of the cells.[6] The use of collagen scaffolds in orthopedic regenerative medicine in practice has not yet been a success, but much research is being done to address the issues being faced. One large issue is the inability to deliver nutrients and remove wastes due to the lack of vascularization in the engineered scaffold. A technique to avoid this before implantation is through the use of bioreactors, which force the medium through the scaffold. Another technique is through cellular engineering where micro-vessels are constructed which act as capillaries through the scaffold and prevent death of the tissue once implanted. The use of growth factors such as vascular endothelial growth factor or insulin-like growth factor can also improve the vascular potential of collagen scaffolds.[6]

A new concept being applied to the field of orthopedic regenerative medicine is gene therapy, which can be used as a method of enhancing the expression of osteogenic and chondrogenic properties. The technique involves the cells used to later seed the scaffold by introducing specific DNA sequences through plasmid DNA transfection into, for example, the genome site which codes for osteo- and chondrogenic genes that promote tissue formation and healing[6] or at the genome site of bone morphogenic protein, which directs the differentiation of stem cells towards osteoblasts and chondrocytes.[11] The plasmid DNA must have a sustained release in order to achieve long term gene expression and healing at the implantation site. This can be done with proper degradation of the collagen scaffold, which would protect internal plasmid DNA resulting in slower, long-term gene expression. Different delivery methods are currently being studied including a gene activated matrix, and viral and non-viral infecting agents. The viral agents include retroviruses and adenoviruses as they have an inherent ability to invade cells and insert their DNA into the host cell genome. The non-viral agents are compounds that form a complex structure with DNA and are less effective yet safer than the viral agents. Elements to improve these carriers are antibodies and proteins, which can bind to the surface of target cells and also improve passage through cell membrane, intracellular tracking, and nuclear targeting.[11] Collagen scaffolds work well as a gene activated matrix due to its hydrophilic properties and ability to bind with many different molecules. Thus, plasmid DNA complexed with viral or non-viral agents can be incorporated with the porous collagen scaffold.[6] Further development of The Human Genome Project could lead to the ability to detect certain diseases in one's genome such as osteoporosis and osteoarthritis. Prior knowledge of these destructive diseases would bring huge improvements to drug development and therapy and also change the way the diseases are treated.[11] Stem cell therapy is another concept being adapted towards orthopedic medicine that has great potential. Mesenchymal stem cells are produced in the bone marrow and studies are being done to better understand their differentiation and transdifferentiation, or the change from one cell type to another, into osteoblasts, chondrocytes, and adipocytes.[11] A better understanding of these gene and stem cell therapies could lead to all new realms of complete tissue regeneration yet to be discovered.

Much more research in this field will lead to more sophisticated and complex bioactive materials that contain bioinstructive and stimuli-responsive characteristics. The use of growth factors and gene therapy is the most likely route towards this achievement.[6] Collagen scaffolds have the all the required properties to use with these advancements in orthopedic regenerative medicine and other tissue sites yet to be discovered.

Nano-Orthopedics

Technology has been allowing for devices in many aspects of our lives to be made smaller and smaller, and orthopedics is no exception. The field of Nano-Orthopedics is quickly growing and is resulting in more accurate development of orthopedic implants. The smaller nanoscale materials are a more appropriate size for connection with biological structures like proteins and ligands than the traditional microscale materials of metallic implants.[11] Like most aspects of medicine, there are road blocks slowing the growth of Nano-Orthopedics that are currently being studied. One such issue is bodily reactions to implants. The use of carbon nanofibers/nanotubes in implants is new to orthopedics yet has shown improved osteoblasts functions and decreased the bodily reaction of fibrous encapsulation of the implant. Carbon nanotubules can be treated chemically with Calcium ions, which help with the crystallization process and also increase the nanotubules biocompatibility. Aligning the nanotubules in the same direction by either passing electricity through them or placing them in a grid can increase their strength. Future research will look at combining the methods to maximize adhesion and new bone growth. It is thought that carbon nanotubules can lead to improved artificial bone flexibility, new bone grafts, and new treatments in osteoporosis and fractures, though more research is needed to understand the body's immune response to the material.[9] Another structural technology is called superlattice coatings, which are nanostructures composed of alternating layers of different materials that have extreme hardness and wear resistant features. This technology is expected to be especially useful in spinal implants due to their wear resistance though it will likely be applied to many areas of orthopedics.[9] Another issue being evaluated in Nano-Orthopedics is increasing the activity of bone cells on implants to induce integration of the implant with the surrounding bone or tissue. If accomplished, additional bone matrix will be produced onto existing bone and the implanted prosthetic leading to a stronger interface between materials.[9]

Nanobone implants are another topic of Nano-Orthopedics that has been designed to have a similar structure to bone. Nanobone comes in a gel form containing tiny nanofibers, which can be injected into a broken bone and assist in the fracture repair process. The gelatinous scaffold replicates the microstructure of cancellous bone and in studies it allowed for osteoblasts to connect with and spread throughout the scaffold. The nanobone material degrades around six months after implantation at which point the space the scaffold once inhabited is replaced by natural bone.[9] This technique is a more positive approach to implantation than ceramic or titanium materials since it avoids infection leading to reoperation and also promotes bone re-growth.

Nanotechnology also shows promise in engineering replacement cartilage in joints. It provides functional scaffolds the ability to promote the growth and differentiation of stem cells. Further research is required to optimize the condition of the surroundings and the degradation rate of the scaffold. Finally, nanotechnology has helped improve arthroscopic surgery as it was used in the development of the Scanning Force Arthroscope which involves only one tube for both visualization and manipulation during surgery instead of two.[9] Nano-Orthopedics is still a new, growing field that certainly has a promising future in medicine.

Biodegradable Orthopedic Implants

A more extensive look at biodegradable orthopedic implants is important because of the amount of attention they receive as a future alternative to current titanium and ceramic implants. Reasons for this include that biodegradable implants provide temporary support to bones but can begin to degrade as new bone tissue is forming. This would drastically reduce the need for secondary surgeries to remove or repair previous implants.[10] Great economic benefits would be gained as well due to decreases in operation time and loss of work time for the patient. Another great benefit of Biodegradable Osteosyntheses (bone implants) specifically is they don’t interfere with radiology treatments, computer tomography, or MRI’s and they result in much fewer infections and sensitivities in the body compared to current titanium implants. Osteosyntheses have also been shown to prevent issues with osteoporosis as they are more efficient at load transferring to the bone than titanium implants so not as much force is transferred to the weak bone.[5] Another great benefit is that biodegradable implants can serve as a scaffold to seed with cells, bioactive molecules, and/or drugs to improve and accelerate the healing process.[10] A few points must be addressed by future research to bring this technology to the forefront. The clear first task is designing the material to degrade at an appropriate rate so that is works as a temporary support yet still allows space for new tissue to grow. Next, it is important that the implanted biomaterial and the degraded material do not create inflammatory or immunogenic bodily reactions. Lastly, the biodegradable implant should have the necessary mechanical strength during the healing process yet be able to decrease its strength and the material degrades so that the mechanical stress can be applied to the new tissue which results in more efficient tissue remodeling.[10]

There are many applications for biodegradable orthopedic implants such as internal fixation devices, scaffolds to induce cell migration, or specific delivery of cells and bioactive factors to help with healing. Biodegradable materials have been used in many fixation forms such as screws, staples, pins, rods and suture anchors, which all must have high load capacity and degradation rates. Poly L-lactide screws are one example of currently studies materials with the necessary strength and load capacity.[10] In addition to providing support; some biodegradable scaffolds also are used as a controlled release agent of bioactive molecules or medications, which are thus delivered right to the defect site. One such bioactive molecule is Bone Morphogenic Protein-2, which has been shown to greatly improve the healing rate of bone both in tissue and biomechanical properties.[11]An example of a medication that can be delivered right to the injury site is a synthetic peptide drug called Chrysalin, which has been shown to improve bone formation by imitating the effects of thrombin and activating the body's natural healing pattern. The study showed that the use of Chrysalin provided increases in bone mineral density, consolidation, and remodeling.[11] The use of a protein coating around the scaffold could be used for better tissue implantation with the live tissue and could also control the release of growth factors and cytokines to aid with tissue healing and regeneration.[15] One structure type used as a controlled release agent is Nano- or microparticles, which is the most popular for bioactive molecule delivery and can be formed by several methods that determine its delivery method. A few methods of formation are single or double emulsion, or by solvent evaporation-extraction techniques. When formed by natural materials, the bioactive molecules are released as the implant degrades while if it is formed with artificial materials, they are released by diffusion to the surrounding structures.[10] Hydrogels are another type of delivery scaffold that is chemically cross-linked and filled with water that can trap medications inside and perform a controlled release. The most enticing benefit of hydrogels is their ability to be injected which allows for minimally invasive therapies. One example of a hydrogel is called oligo-poly ethylene glycol fumarate, which is a carrier of growth factors for cartilage and bone tissue engineering.[10] A final application of biodegradable orthopedic implants is as a cell carrier to help with tissue regeneration. Scaffold used to carry cells generally have intricate pore structures throughout, which can be created with techniques such as phase separation, solvent casting, particulate leaching, or electrospinning. The pore structure is very important in order to allow nutrient exchange and cellular adhesion. In vitro bone formation experiments have successfully resulted in osteoblasts growth and cell differentiation.[10]

Biodegradable orthopedic implants also have many requirements, which are being researched that they must meet in order to function properly. These requirements include biocompatibility, biodegradability, biological properties, mechanical properties, and also the ability of the materials to be processed. The biocompatibility of a scaffold is based on its chemical make-up and also the way it was processed. Having a biocompatible implant is important to avoid inflammatory and immunogenic responses in the body both as an implant and during the degradation stages.[10] Effects from low pH have brought about studies trying to resolve the problem by loading the implant with basic salts to balance the pH. Ossification around the implant is also an issue that has been reduced in some studies that load the implants with recombinant human fibroblast growth factor-2.[5] The biodegradability of these implants is arguably the most important property as it is the innovative ability that removes the need for secondary removal surgery and also promotes the re-growth and strengthening of the injured site. The rate of biodegradability is also an important factor as it must be matched with the growth rate of the tissue it is implanted into to ensure a proper maintenance and transfer of strength throughout the healing process. Degradation of biodegradable implants occurs naturally in the body over time through hydrolysis or enzymatic breakdown.[10] The biological properties of biodegradable orthopedic implants are important because they don't serve simply as a tissue replacement but also as a method of increasing tissue healing and growth. Biological factors that are added to the implants can help improve its osseous fixation and bacterial resistance.[11]The specific site of an implant is what determines the mechanical requirements of the implant. Bone implants must be hard and stiff to withstand load bearing while cartilage tissue requires viscoelastic properties to withstand friction and compressive forces. A new area of research that could allow a more specific look at tissue properties is *in vivo* kinematics. This is the measurement of movement within living tissue, which could collect data at a certain tissue site and record the type and amount of force experienced there so that a customized scaffold could be made for just that tissue.[15] Right after implantation is the most critical time for good mechanical properties of the implant as it is responsible for the majority of the load. As the implant degrades, it must have a gradual decrease in strength to allow for a smooth transfer of the load from the implant to the new tissue.[10]The size and amount of material used in biodegradable implants should be as low as possible since the goal is for them to eventually degrade. Some studies have shown increases in bending and shear strength by orienting fibers and molecules together within an implant. Some implants combined with rubber have shown an increased toughness that avoids brittleness seen without rubber.[5] Though, the more natural the materials in the implant are, the more it encourages cellular adhesion and tissue growth. The processability of biodegradable implants is another important factor in order to maintain a low infection rate though sterilization and also provide ease of implantation. Factors affecting ease of implantation include viscosity, curing time, and implant shape which all must be optimized before an implant can be surgically installed. Sterility is a vital property of scaffolds but doing so without any change to the composition and shape isn’t an easy task. Many common heat and moisture sterilization techniques have negative effects on the physical and mechanical properties of biodegradable implants.[10] Some new sterilization techniques are being developed to avoid disrupting the properties of implants such as low-temperature plasma treatments, which resulted in no change of the mechanical properties and only slight changes in the molecular weight and crystallinity of the implant. One sterilization technique has received modifications to reduce harmful implant effects and is known as steam sterilization. The modifications include much shorter cycle durations and the exposure to moisture is much lower. This resulted in quite a bit of molecular weight loss yet little change in mechanical properties. A final sterilization technique being studied is autosterilization through injection molding, so as the implant is being heated and molded into shape, the sterilization occurs at the same time.[5]

Biodegradable orthopedic implants show great promise as a replacement of current implants in the future. They show greater compatibility and their ability to self-degrade results in less surgical time and allows the body more autonomy in healing itself back to normal. Though they are still in the early stages of development, biodegradable scaffolds show they are a great aid to orthopedic injury and that future research in this field could lead to complete regeneration of orthopedic tissues.[10]

Robot-Assisted Orthopedic Surgery

A new technology that continues to evolve is robot-assisted orthopedic surgery. There are three main benefits provided by robot assistance over non-robot surgery including greater precision than a human alone, programmable to produce consistent results, and greater spatial accuracy with dynamic scanning and positioning technology.[1] Robot-assisted orthopedic technology is an advancement of computer assisted, which is always controlled by the surgeon and is generally used to provide positioning information of the instruments relative to the patient anatomy. Orthopedic robot systems are broken into four types; passive, active, positioning aids, and cutting aids. The difference between passive and active systems is the amount of control given to the device. Passive systems are under complete control by the surgeon yet require anatomical positions be registered before machining begins. Active systems, on the other hand, have some range of autonomy and can spatially orient themselves before making the programmed moves and cuts. Positioning aids help rotate and keep a bone in place and cutting aids make the programmed cuts once positioned by the surgeon.[1] There are many advantages and disadvantages of robot-assisted orthopedic surgery. A few advantages include being able to securely attach to rigid bone structures, bone is a dense structure which is easy to be scanned by the robot, bone can be easily manipulated and fixed into position, and robot devices are capable of producing the high energy forces needed for orthopedic surgery. Some disadvantages are that current robotic technology results in longer surgeries due to the necessary scanning and positioning measures, the equipment is very expensive, and they can be difficult to learn how to use.[1] The technology making robot-assisted orthopedic surgery such a lucrative idea is the ability to abort an active system's plan and its positioning system, which uses optical cameras, infrared diodes, magnetic and mechanical bone motion sensors.

There are several specific areas of the body that are being looked at to improve the use or for future use of robot-assisted orthopedic surgery. The hip and knee joints are great candidates for its use because the massive long bones associated with the joints are easy for robots to attach to. The use of robotics during total hip and knee replacements has been shown to result in a more accurate placement of the implanted stem and thus greater contact, healing, and growth of the implant site. Robotic milling of bone at the implant site is also improved and results in a more stable and functional implant.[1] Knee ligament injuries are another site for use of robot-assisted orthopedic surgery. Research is looking at the use of robotics to increase the accuracy of tunneling done in the tibia and femur for placement of the ACL and PCL during reconstructive surgery. They are finding that the robotics are creating tunnel directions, which are as consistent as the most experienced surgeons, though further research is being done to increase the role of robotics in ligamentous surgery.[1] Spine and trauma injuries have some minimal use currently for robot assisted orthopedic surgery, but the potential uses are glaring once the control and accuracy of smaller scale robots can be obtained due to the amount of care needed for these surgeries.

The numerous coinciding needs and abilities of orthopedic medicine and robotic technology such as strong fixation for positioning, cutting, and drilling make the two a perfect match. The accuracy and improved outcomes of robotic surgery has been seen in several orthopedic areas with many more to come in the future. Robotics is an enhancement technology when paired with orthopedics because it allows all surgeons to achieve the same level of precision and accuracy when making cuts or placing implants. Surgical teams can virtually plan out their entire procedure and have the robot pre-programmed to match that operation. Some issues must still be addressed before their use is expanded. These include safety, liability, credentialing, training for use, and continuing improved patient outcomes. Cost is also a major issue that will likely decrease with the advancement of technology, but that will require the cooperation of many groups such as surgeons, engineers, computer scientists, and imaging specialists in order to improve their use. These improvements will lead to more user friendly, less invasive, and hopefully less expensive orthopedic robot in the future that could change the way orthopedic surgery is done.[1] The benefits brought upon by this technology are astounding and its potential may be more than one could ever foresee.

Future of the Orthopedist

Orthopedics is changing in many ways thanks to the influential developments in microsurgery, tissue engineering, genomics, nanotechnology, computer and robot-assisted surgery, and pharmaceuticals.[16] The providers of orthopedic medicine are no exception to change in their field. One of these changes coming for Orthopedists is the need for them to contribute more towards research, both clinically and at the basic science level. Their involvement is vital to the growth of the field as biological researchers and engineers cannot guide the field towards new developments alone. An interdisciplinary team of clinicians, biologists, and engineers should be created to bridge the gap between clinical and research science. Surgeons working collaboratively with engineering companies must continue to focus on creating implants and devices with the greatest functional outcomes while ensuring their efficacy, safety, and cost-effectiveness.[3] A realistic connection must be made between post-residency research and clinical careers which can begin with a creation of a clinical research database that includes the treatment information of all patients so that discoveries made during treatment can be attributed to furthering evidence based practice.[13] Research in both basic and clinical settings is the key to new developments in orthopedic medicine.

The workload for orthopedists is also on the rise. Studies are projecting the number of hip and knee replacements to soar by the year 2030 as people will continue to live longer, but experts hope that increased operative efficiency, technical capacity, and improved implant longevity can alleviate some of the supply and demand discrepancy.[3] A trend towards further specialization in orthopedic medicine, with a majority going into sports medicine or hand surgery, is leading to a decrease in general orthopedic surgeons, which is also a concern.

The effort to persuade clinicians to increase their participation in research has been a difficult task. The Orthopedic Research and Education Foundation believes this task is the method of 'discovering' the future of orthopedic medicine and they have been showing and giving support for that research and the researchers who are willing to make that discovery. OREF has been encouraging research from young orthopedic residents through Resident Research symposia where the resident's research is presented and evaluated by surgeons and basic scientists.[16] Events like this could help influence the residents to continue their participation in research throughout their career. OREF unfortunately can only fund about 50% of the qualified grant applications they receive for research, so even when participation is present, funding isn't always.

The Journal of Bone and Joint Surgery performed an interesting study in which they attempted to identify the factors that may influence orthopedic residents' intent to perform research. The primary goals of their study included to see if residents and chair members realize the importance of research, find the portion of residents who have some interest to perform research, find which factors influence their interest to perform research, and to compare those factors with the opinions of chair members who have control over the factors.[2] The results showed that 99% of residents felt research was important and 42% were likely to perform research in the future. They also found that 70% were willing to or indifferent to research, which the study denoted as the enticeable crowd. The incentives to participate in research that were rated the highest by residents were total educational debt forgiveness along with a full time clinician's salary. This differed greatly from the incentives chosen by the chair members. An optimal set of incentives compromised between the residents and chairs would include a combination of protected time, increased funding, salary support, and debt relief.[2] Unfortunately, the majority of respondents admitted they weren't willing to help fund research at their personal or departmental expense. This research has reiterated the fact that it's imperative for orthopedic leadership groups to continue to provide incentives to the enticeable clinicians so that research continues to be produced.

In conclusion, orthopedic medicine has some impressively innovative changes coming in its not too distant future. The collaboration between teams of scientists, researchers, and engineers has developed some remarkable new techniques and devices along with a few great adaptations to current treatment options. Further advances in science and technology fields such as stem cells, imaging technology, functional tissue engineering, and robotic assistance will further propel the diagnostic and treatment abilities of orthopedic medicine.[15] More advancements will be required in order to provide less invasive and faster recovering treatment options to our vulnerable aging population. The pathway to new advancements in orthopedic medicine is through research, which must continue to be encouraged and funded as it is the key to the future of orthopedic medicine.

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