



Ministry of Highe  
Edcation Uuniversity  
Hill College University  
Department Medical Physics



## Bone and joint problem

بحث مقدم إلى :

كلية الحلة الجامعة – قسم الفيزياء الطبية

وهو جزء من متطلبات نيل درجة البكالوريوس في الفيزياء الطبية

إعداد الطلبة :

زهراء قاسم صالح محمد علي حسين

عباس اسماعيل ابراهيم محمد خضر علي

حيدر ضرغام عزيز

بإشراف :

م.م نورس بهاء

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ  
(يَرْفَعُ اللَّهُ الَّذِينَ آمَنُوا مِنْكُمْ وَالَّذِينَ أُوتُوا  
الْعِلْمَ دَرَجَاتٍ)

صَدَقَ اللَّهُ الْعَلِيِّ الْعَظِيمُ

(المجادلة: ١١)

## الإهداء

لم تكن الرحلة قصيرة ولا الطرق مخوفاً بالتسهيلات لكنني فعلتها فالحمد لله الذي يسر البدايات  
وبلغنا النهايات

ها أنا اليوم أقف على عتبة تخرجني أقطف ثمار تعبتي وأرفع قبعتي بكل فخر ، فاللهم لك الحمد  
قبل أن ترضى ولك الحمد إذا رضيت ولك الحمد بعد الرضا ، لأنك وفققتني على اتمام هذا  
النجاح وتحقيق حلمي ...

أهدي ثمرة نجاحي وتخرجي والجهد المبذول في السنين الماضية الى بقية الله الاعظم صاحب  
العصر والزمان الامام الهادي المهدي (عجل الله تعالى له الفرج )

أهدي هذا النجاح لنفسي الطموح ، ثم إلى كل من سعى معي لإتمام مسيرتي الجامعية  
إلى اليد التي أزالته عن طريقي الأشواك ، ومن تحملت كل لحظة ألم مررت بها  
وساندتني وسهرت ليالي طويلة من أجل راحتي واستيقظت فجرا للدعاء لي ....

## الى امي الحبيبة ...

الى الذي زين اسمي بأجمل الألقاب ، من دعمني بلا حدود وأعطاني بلا مقابل ، الى من علمني  
أن الدنيا كفاح وسلاحها العلم والمعرفة، داعمي الأول في مسيرتي وسندي وقوتي وملاذي بعد  
الله فخري واعتزازي

## : والدي

إلى الذي غمروني بالحب والتوجيه وأمدني دائماً بالقوة وكانوا موضع الاتكاء في كل عثراتي  
وإذنين رزقني الله بهم لأعرف من خلالهم طعم الحياة إلى

## : اصدقاء العمر

إلى الدكتورة التي ألهمتني وحببتني بالتخصص... كلمة شكرا لا توفيتها ، كانت بصمة جميلة في  
حياتي الجامعية أسأل الله كل التوفيق لها

## مقررة القسم : زهراء نجاح

## شكر و تقدير

الحمد لله الذي من عليه بفضلة وكرمة والصلاة على خير خلقه الحبيب المصطفى  
واله الاطهار وصحبة المنتجبين الابرار لمن دواعي الفخر ان أتقدم بالشكر و التقدير  
لكل من ساندني وساعدني وشجعني لخوض غمار هذه المرحلة

ولابد لنا ونحن نخطو خطواتنا الأخيرة في الحياة الجامعية من وقفة نعود إلى

أعوام قضيناها في رحاب الجامعة مع أساتذتنا الكرام الذين قدموا لنا

الكثير باذلين جهودا كبيرة في بناء جيل الغد لتبعث الأمة من جديد...

وقبل أن نمضي نقدم أسمى آيات الشكر والامتنان والتقدير والمحبة إلى

الذين حلوا أقدس رسالة في الحياة ....

إلى الذين مهدوا لنا طريق العلم والمعرفة ....

ثم يسعدني التقديم بجزيل الشكر والامتنان لكل من ساندني وأعانني في إتمام هذا  
المشروع وأولهم أستاذتي الفاضلة **نورس بهاء** التي كانت لطفا بقبول إشرافها على  
بحثي وكانت دأبتاً في توجيهات قوية لإثراء هذا البحث فقد استفدتُ من خبرتها  
المتوخية في هذا المجال وأستفاد من حكمته في التعامل معنا

فجزى الله خيراً لأستاذتي الموقرة حفظها الله تعالى

كذلك نشكر **كلية الحلة الجامعة** التي منحتني فرصة الدراسة في **قسم الفيزياء الطبية**  
الذين لم يبخلوا لا بالجهد ولا بالوقت اذ كانوا يخجلوننا بحرصهم علينا لبذل جهد  
مضاعف فهذا الشكر قليل بحقهم لرد من جميلهم لإنجاز هذا البحث ..

وفي الختام اتقدم بالشكر الجزيل الى كل من ساهم بشكل او باخر في انجاز هذا  
البحث.

## Summary

A bone is a solid organ that forms part of the skeleton. It supports the body and protects the various organs of the body. It produces red blood cells and white blood cells, stores minerals, provides support for the body. Types of bones long bone. Short bones. Flat bones. Irregular bones. A joint is a point where two bones make contact. Joints can be classified either histologically or functionally.

Bone disorders is the most well differentiated organ that originates from mesenchyme tissue is primarily a structural load-bearing organ. It provides protection to vital organs.

Diagnosis as the initial step of medical practice, is one of the most important parts of complicated clinical decision making which is usually accompanied with the degree of ambiguity and uncertainty .Diagnosis of arthritis in general, methods of treating it, as well as ways to prevent arthritis.

People with arthritis are at high risk of developing other diseases, including heart disease Arthritis is a progressive autoimmune disease characterized by severe swelling and pain in the joints Osteoporosis is a serious public health problem worldwide. It is common in older people and requires screening and recommended treatment to prevent disease progression.Preventing cancer is by taking nutritional supplements that contain vitamins, especially vitamin D, and drinking green teaOsteoporosis can be hereditary through osteogenesis imperfecta that results from collagen-related defects. disease modifying antirheumatic drugs. Monitoring rheumatoid arthritis Treatment of Selected Bone Cance. Osteosarcoma. treatment .

X-rays of joints and bones are a common imaging technique used to diagnose various conditions and injuries. They provide detailed images of bones, joints, and surrounding tissues, helping healthcare professionals assess for fractures, arthritis, bone infections, and other abnormalities. X-rays are quick, non-invasive, and readily available, making them an essential tool in orthopedic diagnosis and treatment planning.

| NO.   | Subject  | Page |
|-------|--|------|
|       | Summary  | I    |
| 1     | Introdcution   | 1    |
| 1.1   | Bone   | 1    |
| 1.2   | Joint  | 3    |
| 2     | Bone Disorders   | 4    |
| 3     | Diseases Related To The Joints   | 5    |
| 3.1   | Rheumatoid Arthritis   | 5    |
| 3.2   | Osteoporosis   | 6    |
| 3.3   | Bone Cancer  | 8    |
| 3.3.1 | Bone Sarcoma   | 8    |
| 3.3.2 | Ewing Sarcoma  | 8    |
| 3.3.3 | Chondro Sarcoma  | 9    |
| 3.4   | Osteogenesis Imperfecta  | 9    |
| 4     | Methods of diagnosing joint diseases   | 10   |
| 5     | Preventing joint disease   | 12   |
| 5.1   | prevention of osteoporosis   | 14   |
| 5.2   | prevention of osteogenesis imperfect   | 15   |
| 6     | Treatments joint and bone diseases   | 16   |
| 6.1   | Rheumatiod arithritis treatment optio  | 16   |
| 6.2   | Treatment of Selected Bone Cancer  | 18   |
| 6.3   | New types of treatment are being tested in clinical trials   | 20   |
| 6.4   | Radiation therapy  | 21   |
| 6.5   | Chemotherapy   | 21   |
| 7     | The effect of physical therapy on joint and bone diseases  | 22   |
| 7.1   | A comparison of two manual physical therapy approaches and electrotherapy modalities for patients with knee osteoarthritis | 25   |

|       |   |    |
|-------|---|----|
| 7.2   | Types of physical therapy for bone and joint diseases | 27 |
| 7.2.1 | Rheumatoid Arthritis                                  | 27 |
| 7.2.2 | Osteoporosis  | 27 |
| 7.2.3 | Bone cancer   | 28 |
| 7.3   | Physical therapy devices                              | 29 |
| 7.3.1 | Transcutaneous electrical nerve stimulation           | 29 |
| 7.3.2 | Electric massager device                              | 30 |
| 7.3.3 | Infrared massage devices                              | 30 |
| 7.3.4 | Ultrasound physical therapy                           | 31 |
| 8     | x-rays of joints and bones                            | 32 |
| 8.1   | X-rays  | 32 |
| 8.2   | Effects of X-rays on bone                             | 34 |
|       | References  | 35 |

# 1.Introduction

## 1.1 Bones

A bone is a solid organ that forms part of the skeleton. It supports the body and protects the various organs of the body. It produces red blood cells and white blood cells, stores minerals, provides support for the body, and enables movement. Bones take many shapes and sizes and have a complex internal and external structure, although bones are light, yet strong and solid, and perform many functions {1}.

Bone tissue is a hard tissue, a type of dense connective tissue, and has a honeycomb-like cellular substance on the inside, which helps solidify the bones. Bone tissue consists of many types of bone cells. Osteocytes and osteoblasts participate in the formation and mineralization of bone, while osteoclasts participate in its absorption. Modified osteoblasts become the lining cells that form a protective layer on the surface of the bone. The mineralized cellular matrix of bone tissue has an organic component, mainly collagen, and an inorganic component, bone mineral, consisting of various salts. Bone tissue is mineralized tissue of two types, cortical bone and cancellous bone. Other types of tissue found in bone include bone marrow, endosteum, periosteum, nerves, blood vessels, and cartilage{2}.

Bone is a metabolically active tissue composed of multiple types of cells. These cells include osteoblasts, which are involved in making and mineralizing bone tissue, osteocytes, and osteoclasts, which are involved in bone resorption. Osteocytes and osteoblasts are derived from bone progenitor cells, while osteoclasts are derived from the same cells that differentiate to form macrophages and monocytes. Hematopoietic stem cells are also found in the bone marrow. These cells give rise to other cells, including white blood cells, red blood cells, and platelets{3}.

There are over 270 bones in the human body at birth, but many of them fuse together during development, leaving 206 separate bones in an adult, and that's not counting the many small sesamoid bones. The largest bone in the body is the femur, while the smallest is the stapes in the middle ear {4}.

Bone is not uniformly solid, but rather contains a durable cellular substance. This cellular material makes up about 30% of the bone, while the remaining 70% consists of salts that give it strength. The cellular material consists of approximately 90-95% of collagen fibers, while the matrix makes up the remaining percentage. The primary tissue of bone, the osteocyte, is relatively tough and lightweight. Its cellular material is composed mostly of a composite material that includes inorganic calcium phosphate in the chemical structure called calcium hydroxylapatite (this is the bone mineral that gives bones their rigidity) and collagen, an elastic protein that increases resistance to fractures. Bone collagen is known as osteonin. Bone is formed by the hardening of that cellular material around the retaining cells. When these cells become sequestered, they transform from osteoblasts into bone cells{5}.

Bone marrow, also known as red bone marrow, can be found in hardly any bone that contains spongy bone. In newborns, all these bones are filled with only red marrow or hematopoietic marrow, but as the child grows older, the hematopoietic ratio decreases in quantity while the fat/bile ratio increases in quantity. In adults, red bone marrow is often found in the bone marrow of the femur, ribs, vertebrae, and hip bones{6}.

## Types of bones

### 1-Long bones

Such as the femur and tibia in particular, undergo the most loads during daily activities and are essential for skeletal movement. Long bones grow primarily by elongation of the diaphysis (the body of the bone) with an epiphysis at each end of the growing bone. The ends of the epiphyses are covered by hyaline cartilage (meniscus). Longitudinal growth of long bones is the result of endochondral ossification of the epiphyseal plate. Bone growth in length is stimulated by the generation of growth hormone (GH) from the secretion of the anterior lobe of the pituitary gland{7}.

### 2- Short bones

Are those whose length is approximately the same as their width. Their primary function is to provide support and stability with little or no movement. Examples

of these bones include the tarsal bones in the foot (tarsus or Achilles bones) and the tarsus bones of the hand {8}.

### 3- Flat bones

Are bones whose function is either extra wide protection or providing broad surfaces for muscle attachment. These bones consist of two thin layers of compact bone (cortical bone), sandwiched between them a variable amount of cancellous bone, which is the site of red bone marrow. In adults, most red blood cells are formed in flat bones {9}.

### 4- Irregular bones

Are bones that, by their composition, cannot be classified as long, flat, or short bones, or even as sesamoid bones. Bones are composed of spongy tissue with cortical (compact) bone. There are also non-appropriate bones to connect all parts of the horse geni, as the horse geni is the place where inappropriate bones can be observed on the human body. This includes indirect bones: human bones, vertebrae, coccyx, and jaw {10}.

A sesamoid bone is a small bone commonly found embedded within a muscle or tendon near joint surfaces, existing as focal areas of ossification and functioning as a pulley to alleviate stress on that particular muscle or tendon. Unlike standard bones, which connect via joints, sesamoid bones connect to muscles via tendons.. Sesamoid bones are most commonly located in the foot, hand, and wrist; the largest and most well-known is the patella. There are many sesamoid bones in a person, with up to 42 reportedly found in an individual Sesamoid bones relieve tension within muscles and tendons, allowing for increased weight-bearing and tolerance by redistributing forces throughout a muscle or tendon, thereby protecting them from significant strain and injury {11}.

## 1.2 Joints

A joint is a point where two bones make contact. Joints can be classified either histologically or functionally. Histological classification is based on the dominant type of connective tissue, and functional classification is based on the amount of movement permitted. Histologically the three joints in the body are fibrous, cartilaginous, and synovial. Functionally the three types of joints are synarthrosis

(immovable), amphiarthrosis (slightly moveable), and diarthrosis (freely moveable). The two classification schemes can be correlated: synarthroses are fibrous, amphiarthroses are cartilaginous, and diarthroses are synovial { 12 }.

Derived from mesenchyme. The bones either develop directly through Joints, comprising bones and connective tissue, are embryologically intramembranous ossification or indirectly through endochondral ossification. Each specific joint has a unique vascular supply and innervation scheme; patterns do exist. Muscles provide stability to joints, and there is a direct correlation between muscle strength and joint stability, particularly with synovial joints { 13 }

## 2. Bone Disorders

Bone is the most well-differentiated organ that originates from mesenchymal tissue. It is alive and dynamic. In terms of function, bone is primarily a structural, load-bearing organ. It provides protection to vital organs and bears loads that the body experiences, both from external forces and those that occur from muscle contraction. Bone provides the anchor point for that muscle contraction through its specialized tendon insertion sites (entheses). Bone's ligament insertion sites, which have the same structure as its tendon insertion sites (and are also classified as entheses), are essential to the function of joints. The articular cartilage that covers the ends of long bones, and which constitutes the bearing surfaces of joints, allows locomotion by the lower extremities and the positioning of the hands in space by the upper extremities. Bone also acts as a metabolic organ in its role as the storage depot of calcium and phosphate. It is the largest reservoir of calcium in the body, and the constant remodeling of bone mobilizes its calcium as one component of the process that tightly mediates calcium homeostasis. Bone remodeling also serves a structural purpose. The remodeling process positions the available mineralized bone tissue in an optimum distribution to bear the loads experienced by the skeleton. The spaces between bony struts and plates that make up trabecular bone (also called spongy or cancellous bone) contain the bone marrow, which produces and stores cells with multiple hematologic and regenerative body functions { 14 }.

### 3. Diseases related to the joints

#### 3.1 Rheumatoid Arthritis

Rheumatoid arthritis (RA) is defined as a systemic autoimmune pathology associated with a chronic inflammatory process, which can damage both joints and extra-articular organs, including the heart, kidney, lung, digestive system, eye, skin and nervous system {15}. Numerous types of arthritis have been investigated and described in order to classify them into non-inflammatory arthritis (osteoarthritis) and inflammatory arthritis caused by crystal deposition (pseudogout, basic calcium phosphate disease, gout), by bacterial and viral infections (Staphylococcus aureus, Neisseria gonorrhoea, complications of Lyme disease, Parvovirus, Enterovirus) or by autoimmune processes {16}. The heterogeneous group of autoimmune rheumatic diseases also includes systemic lupus erythematosus (SLE), Sjögren's syndrome, adult-onset scleroderma, spondylarthritis (SpA), psoriatic arthritis (PsA), polymyositis (PM), etc. Due to the fact that they may be similar in signs and symptoms, differential diagnosis is essential {17}.

Although a number of biomolecular mechanisms have been proposed, the etiology of RA is not yet fully elucidated, a current hypothesis being that dysregulated citrullination leads to the production of anti-citrullinated protein antibodies (ACPAs) {18,19}. The evolution of RA is fluctuant with episodic exacerbations and in the absence of optimal treatment symptoms gradually worsen until the joints are irreversibly damaged and physical and psychological functioning is affected {20}. Moreover, RA complications and comorbidities reduce the life expectancy of patients by a few years {21}.

Due to major advances in the pharmaceutical industry, new therapeutic approaches are available. However, the lack of understanding of the molecular mechanisms governing the fate of antibodies leads to a challenge in order to discover a curative treatment. The most effective therapeutic approach requires early diagnosis and an optimal nonpharmacological and pharmacological treatment, associated with periodic evaluation of therapeutic efficacy and safety. The target of therapy is to obtain remission and to reduce side effects {22}. Pharmacological agents that help maintain joint function can be classified as conventional synthetic disease-modifying antirheumatic drugs (DMARDs),

biologic DMARDs and targeted synthetic DMARDs, which are included in irreversibly. Outcomes have been improved by recognizing the benefits of early diagnosis and early therapy with disease-modifying antirheumatic drugs (DMARDs). The treatment target is remission or a state of at least low disease activity,

which should be attained within 6 months. Methotrexate is first-line therapy and should be prescribed at an optimal dose of 25 mg weekly and in combination with glucocorticoids; 40% to 50% of patients reach remission or at least low disease activity with this regimen. a new class of nonbiologic DMARDs by the American College of Rheumatology (ACR) {23}. Inadequate symptom control in RA patients requires the use of nonsteroidal anti-inflammatory drugs (NSAIDs) and glucocorticoids (GCs) as adjunctive therapy in reducing inflammation {24}.

Early diagnosis and treatment of RA can avert or substantially slow progression of joint damage in up to 90% of patients, thereby preventing irreversible disability. The development of novel instruments to measure disease activity and identify the presence or absence of remission have facilitated new treatment strategies to arrest RA before joints are damaged {25}.

### 3.2 Osteoporosis

Osteoporosis is a disease that is characterized by low bone mass, deterioration of bone tissue, and disruption of bone microarchitecture: it can lead to compromised bone strength and an increase in the risk of fractures {26}.

Is the most common bone disease in humans, representing a major public health problem. It is more common in Caucasians, women, and older people. Osteoporosis is a risk factor for fracture just as hypertension is for stroke {27}.

There are factors associated with an increased risk of osteoporosis-related fractures. These include general factors that relate to aging and sex steroid deficiency, as well as specific risk factors such as use of glucocorticoids (which cause decreased bone formation and bone loss), reduced bone quality, and disruption of microarchitectural integrity. Fractures result when weakened bone is overloaded, often by falls or certain daily chores {28}.

## Classification

Osteoporosis can be classified into two main groups by considering the factors affecting bone metabolism:

- Primary osteoporosis
- Secondary osteoporosis
- Primary osteoporosis can also be divided into two subgroups:

### A. Involutional Osteoporosis Type

It is also known as postmenopausal osteoporosis, caused by the deficiency of estrogen, mainly affecting the trabecular bone; therefore, women are more susceptible to osteoporosis than men, as evident by a men/women ratio of 4/5.7 {29} .

### B. Involutional Osteoporosis Type

It is also called senile osteoporosis, and it is related to bone mass lost due to the aging of cortical and trabecular bones {30} .

- Secondary Different diseases, medications, and lifestyle changes can cause osteoporosis

Causes of osteoporosis include increasing age, female sex, postmenopausal status, hypogonadism or premature ovarian failure, low body mass index, ethnic background (white persons are at higher risk than black persons), rheumatoid arthritis (RA), low BMD, vitamin D deficiency, low calcium intake, hyperkyphosis, current smoking, alcohol abuse, immobilization, and long-term use of certain medications, such as glucocorticoids, anticoagulants, anticonvulsants, aromatase inhibitors, cancer chemotherapeutic drugs, and gonadotropin-releasing hormone agonists {31}.

screening by dual energy X-ray absorptiometry (DEXA) is important to obtain an early diagnosis and to avoid fractures {32}. All women aged 65 years or older and men aged 70 years or older, postmenopausal women with medical causes of bone loss (e.g., steroid use) regardless of age, postmenopausal women aged 50

years or older with additional risk factors for fracture (e.g., current smoker, RA, history of hip fracture in a parent), and postmenopausal women with a fragility fracture should be screened for osteoporosis by BMD measurement at the hip and lumbar spine {33}.

### 3.3 Bone cancer

bone cancer originates from the healthy cells and starts forming a tumor {34}. The primary symptom of bone cancer is a bone tumor. The tumor grows gradually and may spread to the other part of the body. It can destroy the bone tissue and bone becomes weaker. The doctor diagnoses cancer via many tests. The X-ray image diagnosis is used to detect cancer in the human bone. The healthy bone and the cancerous bone X-ray assimilation rates are different. Due to which a cancerous bone image surface appears ragged {35}. The bone cancer severity is measured by a stage and the grade. Tumor (geographic bone destruction) growth rate is used by doctors to predict the disease growth rate {36}.

#### 3.3.1 Bone Sarcoma

usually known as bone cancer, is a rare type of cancer that refersto an abnormal growth of tissue inside the bone, with high probability to spread to other parts of the body. It commonly affects children, teenagers and young adults. As for all other types of cancer (breast, lung, prostate, stomach, brain ...), there are no identified causes for bone cancer. Therefore, only an early detection could help increasing the chances to survive a bone sarcoma. The association of medical imaging modalities (such as X-ray, MRI and CT imaging) with image processing techniques can provide more accuracy while detection eventual bone tumors {37}

#### 3.3.2 Ewing Sarcoma

Ewing sarcoma is the second most common type of bone cancer, comprising about one-third of cases in the United States. Its estimated incidence is one in 100,000 among persons 10 to 19 years of age. It is more common in whites and Asians than in blacks.

The cell origin of Ewing sarcoma is not known. It has been hypothesized that these tumors derive from undifferentiated, primitive neuroectodermal or neural crest cells. Recently, it has been suggested that Ewing sarcoma originates from primitive stem cells, and the degree of malignancy depends on the stage of stem cell arrest during differentiation. Ewing sarcoma is included in a group of tumors known as small blue round cell tumors, based on their microscopic features.

Ewing sarcoma and osteosarcoma have similar characteristics. Ewing sarcoma primarily affects children and adolescents, with a median age of 15 years. Ewing tumors also classically metastasize to the lungs and other bones. A major difference is the anatomic locations in which Ewing sarcomas typically develop: the pelvis, diaphysis of long bones, ribs, and scapula.

### 3.3.3 Chondrosarcoma

Chondrosarcoma is a malignant, cartilage-producing bone tumor. It is the least common bone cancer, with an estimated incidence of one in 200,000 persons. Unlike osteosarcoma and Ewing sarcoma, chondrosarcoma typically manifests in adults 40 to 75 years of age. It occurs more in the central skeleton, commonly arising from the pelvic girdle, vertebrae, and proximal long bones {38}.

### 3.4 Osteogenesis Imperfecta

Osteogenesis imperfecta (OI), or brittle bone disease, is a heterogeneous disorder characterised by bone fragility, multiple fractures, bone deformity, and short stature. OI is a heterogeneous disorder primarily caused by mutations in the genes involved in the production of type 1 collagen. Severe OI is perinatally lethal, while mild OI can sometimes not be recognised until adulthood. Severe or lethal OI can usually be diagnosed using antenatal ultrasound and confirmed by various imaging modalities and genetic testing. The hallmarks of OI are bone fragility, high frequency of fractures, bone deformities, and growth deficiency {39}.

As the production of type I collagen in various tissues is impaired, individuals with OI may also suffer from other clinical symptoms such as brittle teeth, blue sclerae, hearing loss, reduced respiratory function, and cardiac valvular regurgitation. The severity of OI varies from mild to extremely severe, with the most severe form being perinatally lethal {40}.

The clinical features of OI vary in severity from mild to lethal. In 1979, Sillence et al. proposed four categories of OI based on specific phenotypes {41}. OI type I, which is related to a quantitative deficiency of structurally normal collagen, is the mildest form, which is characterised by blue sclerae but no bone deformities {42}.

In contrast, OI types II–IV are caused by structural abnormalities of type I collagen {43}. OI type II is extremely severe and perinatally lethal. OI type III, the most severe form observed in patients who survive the neonatal period, comprises severe progressive deformities and an extremely short stature. OI type IV results in mild to moderate bone deformities, short stature, and normal sclerae {44}.

With an increase in the discovery of the number of gene mutations responsible for causing OI, the classification of OI subtypes has expanded up to OI type XX to date {45}. However, even within the same genetic mutations, various phenotypes are observed; therefore, it is difficult to correlate the molecular genetic classification with the Sillence classification {46}.

#### 4. Methods of diagnosing joint diseases

Diagnosis as the initial step of medical practice, is one of the most important parts of complicated clinical decision making which is usually accompanied with the degree of ambiguity and uncertainty. Since uncertainty is the inseparable nature of medicine, fuzzy logic methods have been used as one of the best methods to decrease this ambiguity. Recently, several kinds of literature have been published related to fuzzy logic methods in a wide range of medical aspects in terms of diagnosis. However, in this context there are a few review articles that have been published which belong to almost ten years ago. Hence, we conducted a systematic review to determine the contribution of utilizing fuzzy logic methods in disease diagnosis in different medical practices {47}.

The sacroiliac joint (SIJ) is a diarthrodial joint that has been implicated as a pain generator in approximately 10% to 25% of patients with mechanical low back or leg symptoms. Unique anatomic and physiologic characteristics of SIJ make it susceptible to mechanical stress and also create challenges in the diagnosis of SIJ pain. A variety of inciting causes for SIJ pain may exist, ranging from repetitive low-impact activities such as jogging to increased stress after multilevel spine

fusion surgery to high-energy trauma such as in motor vehicle accidents. Similarly, wide variability exists in the clinical presentation of SIJ pain from localized pain or tenderness around the SIJ to radiating pain into the groin or even the entire lower extremity. No pathognomonic clinical history, physical examination finding, or imaging study exists that aids clinicians in making a reliable diagnosis. However, imaging combined with clinical provocative tests might help to identify patients for further investigation. Although provocative physical examination tests have not received reliable consensus, if three or more provocative tests are positive, pursuing a diagnostic SIJ injection is considered reasonable. Notable pain relief with intra-articular anesthetic injection under radiographic guidance has been shown to provide reliable evidence in the diagnosis of SIJ pain {48}.

Osteoarthritis (OA) is one of the most common joint diseases, especially in the elderly, with approximately 3 million newly diagnosed cases each year {49}. OA is characterized by cartilage degradation, synovial inflammation, subchondral bone remodeling, and osteophyte formation, which ultimately leads to joint function loss {50}. Currently, the routine diagnosis of OA is usually based on clinical manifestations and joint imaging techniques; thus, a precise early diagnosis of OA is not possible. Because the diagnosis is not established early, the disease progresses for most patients resulting in a poor prognosis and ineffective treatment options. Therefore, exploring biomarkers that would make an early diagnosis possible is crucial for improving the prognosis of OA patients{51}.

Deep learning-based MRI diagnosis of internal joint derangement is an emerging field of artificial intelligence, which offers many exciting possibilities for musculoskeletal radiology. A variety of investigational deep learning algorithms have been developed to detect anterior cruciate ligament tears, meniscus tears, and rotator cuff disorders. Additional deep learning-based MRI algorithms have been investigated to detect Achilles tendon tears, recurrence prediction of musculoskeletal neoplasms, and complex segmentation of nerves, bones, and muscles{52}.

The diagnosis of periprosthetic joint infection (PJI) in the early postoperative period remains a challenge. Although studies have established that serum C-reactive protein (CRP) and synovial markers may be useful, recent studies have suggested that the current thresholds used may lack sensitivity. The purpose of this

study was to examine the role of serum CRP, erythrocyte sedimentation rate (ESR), synovial fluid white blood-cell (WBC) count, and polymorphonuclear neutrophil (PMN) percentage in the diagnosis of acute postoperative PJI and to identify the optimal threshold {53}.

Osteoarthritis (OA) is a very common disease that affects the human knee joint, particularly the articular cartilage and meniscus components which are regularly under compressive mechanical loads. Early-stage OA diagnosis is essential as it allows for timely intervention. The primary non-invasive approaches currently available for OA diagnosis include magnetic resonance imaging (MRI), which provides excellent soft tissue contrast at high spatial resolution. MRI-based knee investigation is usually performed on joints at rest or in a non-weight-bearing condition that does not mimic the actual physiological condition of the joint. This discrepancy may lead to missed detections of early-stage OA or of minor lesions. The mechanical properties of degenerated musculoskeletal (MSK) tissues may vary markedly before any significant morphological or structural changes detectable by MRI. Recognizing distinct deformation characteristics of these tissues under known mechanical loads may reveal crucial joint lesions or mechanical malfunctions which result from early-stage OA. This review article summarizes the large number of MRI-based investigations on knee joints under mechanical loading which have been reported in the literature including the corresponding MRI measures, the MRI-compatible devices employed, and potential challenges due to the limitations of clinical MRI sequences {54}.

## 5. Preventing joint disease

Osteogenesis imperfecta (OI) is the most common inherited form of bone fragility and includes a heterogeneous group of genetic disorders which most commonly result from defects associated with type 1 collagen. 85%–90% of cases are inherited in an autosomal dominant manner and are caused by mutations in the COL1A1 and COL1A2 genes, leading to quantitative or qualitative defects in type 1 collagen. In the last decade, defects in several other proteins involved in the normal processing of type 1 collagen have been described. Recent advances in genetics have called for reconsideration of the classification of OI, however, most recent classifications align with the classic clinical classification by Silvers {55}.

Rheumatoid arthritis (RA) is currently diagnosed and treated when an individual presents with signs and symptoms of inflammatory arthritis (IA) as well as other features, such as autoantibodies and/or imaging findings, that provide sufficient confidence that the individual has RA-like IA (e.g., meeting established classification criteria) that warrants therapeutic intervention. However, it is now known that there is a stage of seropositive RA during which circulating biomarkers and other factors (e.g., joint symptoms) can be used to predict if and when an individual who does not currently have IA may develop future clinically apparent IA and classifiable RA. Indeed, the discovery of the “pre-RA” stage of seropositive disease has led to the development of several clinical trials in which individuals are studied to identify ways to delay or prevent the onset of clinically apparent IA/RA. This review focuses on several issues pertinent to understanding the prevention of RA. These include discussion of the pathogenesis of pre-RA development, prediction of the likelihood and timing of future classifiable RA, and a review of completed and ongoing clinical trials in RA prevention. Furthermore, this review discusses challenges and opportunities to be addressed to effect a paradigm shift in RA, where in the near future, proactive risk assessment focused on prevention of RA will become a public health strategy in much the same manner as cardiovascular disease is managed today{56}.

Rheumatoid arthritis is a progressive autoimmune disease characterised by severely swollen and painful joints. To compliment pharmacotherapy, people living with rheumatoid arthritis often turn to dietary interventions such as the Mediterranean diet. The aim of the present systematic review is to discuss the effects of the Mediterranean diet {57}.

Patients with rheumatoid arthritis (RA) are at high risk of developing cardiovascular disease (CVD). Inflammation has a pivotal role in the pathogenesis of CVD. RA is an inflammatory joint disease and, compared with the general population, patients with RA have approximately double the risk of atherosclerotic CVD, stroke, heart failure and atrial fibrillation. Although this high risk of CVD has been known for decades, patients with RA receive poorer primary and secondary CVD preventive care than other high-risk patients, and an unmet need exists for improved CVD preventive measures for patients with RA. This Review summarizes the evidence for atherosclerotic CVD in patients with RA and provides a contemporary analysis of what is known and what needs to be further clarified

about recommendations for CVD prevention in patients with RA compared with the general population. The management of traditional CVD risk factors, including blood pressure, lipids, diabetes mellitus and lifestyle-related risk factors, as well as the effects of inflammation and the use of antirheumatic medication on CVD risk and risk management in patients with RA are discussed. The main aim is to provide a roadmap of atherosclerotic CVD risk management and prevention for patients with RA {58}.

## 5.1 prevention of osteoporosis

Osteoporosis is a serious public health concern worldwide, and community-based public health programs that increase osteoporosis preventive behaviors are ideal to combat this major public health issue. A review of community-based public health programs for osteoporosis prevention show that programs vary in numerous ways and have mixed results in increasing osteoporosis preventive behaviors, although most programs have had success in significantly increasing calcium intake, only a few programs have had success in significantly increasing weight-bearing exercise. Regarding calcium intake, all community-based public health programs that implemented: 1) at least one theoretical behavior change model, such as the health belief model, or 2) bone mineral density (BMD) testing for osteoporosis screening, have shown success in significantly increasing calcium intake. As community-based public health programs for osteoporosis prevention have shown limited success in increasing weight-bearing exercise, an additional review of community-based public health programs incorporating osteoporosis exercise showed that they have high compliance rates to increase weight-bearing exercise, but require high-intensity weight-bearing exercise of 80–85% 1-repetition maximum to significantly increase BMD to prevent osteoporosis. In the prevention of osteoporosis, for community-based public health programs to be most effective, they should implement theoretical behavior change models and/or BMD testing for osteoporosis screening, along with high-intensity resistance training. Recommendations for future research to further study effective community-based public health programs are also provided{59}.

Osteoporosis and sarcopenia are common in older adults. Osteoporosis is a systemic skeletal disease characterized by low bone mass and microarchitectural deterioration of bone tissue, with a consequent increase in bone fragility and

susceptibility to fracture. Bone fractures can result in changes in posture, pain, the need for surgical repair and functional impairment. Sarcopenia is the progressive and generalized loss of skeletal muscle mass, strength and/or physical performance. Older adults with sarcopenia experience increased risk of frailty, disability, hospitalizations, mortality, and a reduced quality of life. In this narrative review we provide guidance regarding the prevention of both osteoporosis and sarcopenia, including interventions that prevent both conditions from occurring, recommended screening and treatment to prevent progression{60}.

## 5.2 prevention of osteogenesis imperfect

Fractures in patients with osteogenesis imperfecta (OI) are caused by a decreased strength of bone due to a decreased quality and quantity of bone matrix and architecture. Mutations in the collagen type 1 encoding genes cause the altered formation of collagen type I, one of the principal building blocks of bone tissue. Due to the complexity of the disease and the high variation of the clinical problems between patients, treatment for these patients should be individually tailored. In general, short immobilization periods with flexible casting material, use of intramedullary implants, and simultaneous deformity correction are preferred. Multidisciplinary care with a broad view of the support needed for the patient and his/her living environment is necessary for the optimal rehabilitation of these patients. Increasing bone strength with exercise, medication, and sometimes alignment surgery is generally indicated to prevent fractures{61}.

Mutations in the two genes coding for collagen type I, COL1A1 and COL1A2, are the most common cause of osteogenesis imperfecta. In the past 10 years, defects in at least 17 other genes have been identified as responsible for osteogenesis imperfecta phenotypes, with either dominant or recessive transmission. Intravenous bisphosphonate infusions are the most widely used medical treatment. This has a marked effect on vertebra in growing children and can lead to vertebral reshaping after compression fractures. However, bisphosphonates are less effective for preventing long-bone fractures. At the moment, new therapies are under investigation.Summary{62}.

Osteogenesis imperfecta (OI) is the term used to describe a group of rare inherited skeletal disorders characterized by a greatly increased risk of fragility

fractures (1). Mutations in several genes can cause OI but the condition is most commonly caused by mutations of COL1A1 or COL1A2 resulting in the production of collagen which is abnormal or present in reduced amounts. Fractures in OI are particularly common during childhood but the elevated fracture risk continues throughout life. Bone mineral density (BMD) can be reduced in OI but the magnitude of increase in fracture risk is far greater than can be accounted for by low BMD, highlighting that a key mechanism of bone fragility is reduced bone quality due to defects of bone matrix and mineralization. A multidisciplinary approach is needed to optimize management of OI, with input from physicians, orthopedic surgeons, physiotherapists {63}.

## 6. Treatments joint and bone diseases

### 6.1 Rheumatoid arthritis treatment options

#### 1. disease modifying antirheumatic drugs

Tumour necrosis factor inhibitors (TNFi) were the first biological agents introduced in the treatment of rheumatoid arthritis (RA) {64}.

Tocilizumab, a monoclonal antibody targeting the interleukin-6 receptor, has become available one decade later and has progressively gained its place into RA treatment algorithms. It has now been included in the last 2013 European League Against Rheumatism (EULAR) recommendations as one of the potential first line biologic drugs, alongside TNFi, after methotrexate (MTX) and/or other synthetic disease modifying antirheumatic drugs (DMARDs) failure, a guidance followed by several national rheumatology societies {65}.

Sulfasalazine, a disease-modifying antirheumatic drug (DMARD), has a well established role in the treatment of patients with rheumatoid arthritis, spondyloarthritis, and inflammatory bowel disease—diseases in which therapeutic benefit may primarily derive from the drug's inhibitory effect on tumour necrosis factor (TNF) and prostaglandin synthesis {66}.

Exercise has wide ranging benefits for health and wellbeing. But it is often most difficult for those who need it most, such as patients with osteoarthritis, who often struggle with daily activities because of pain and limited mobility. On April 29, 2022, the UK National Institute for Health and Care Excellence (NICE)

released draft guidance recommending tailored therapeutic exercise, such as muscle strengthening and aerobic exercise, for all patients with osteoarthritis. Although exercise was recommended in previous NICE guidelines, it now takes centre stage over oral analgesics including paracetamol, NSAIDs, and opioids {67}.

Offer short term glucocorticoid treatment for managing flare-ups. In people with established disease . Continue long term treatment with glucocorticoids only after fully discussing with the individual the long term complications of the treatment and after offering all other treatment options (including biological drugs) {68}.

## 2. Monitoring rheumatoid arthritis

Regularly measure C reactive protein and key components of disease activity (using a composite score such as the DAS28—a disease activity score that includes assessment of 28 joints<sup>3</sup> ) to inform decision making about increasing treatment to control disease or cautiously decreasing treatment when disease is controlled. If the disease is of recent onset and active, measure these variables monthly until control reaches a level previously agreed with the individual {69}.

Check for comorbidities such as hypertension, ischaemic heart disease, osteoporosis, and depression -Assess symptoms that suggest complications, such as vasculitis and disease of the cervical spine, lung, or eyes -Organise appropriate cross referral within the multidisciplinary team -Assess the need for referral for surgery {70}.

Offer referral for an early specialist surgical opinion if any of the following do not respond to optimal non-surgical management: -Persistent pain as a result of joint damage or other identifiable damage to soft tissue -Worsening joint function - Progressive deformity -Persistent localised synovitis {71}.

Offer urgent combined medical and surgical management to those with suspected or proved septic arthritis (especially in a prosthetic joint) {72}.

## 6.2 Treatment of Selected Bone Cancer:

### A. Osteosarcoma

Treatment recommendations for stages IA-IB (low grade) osteosarcomas are as follows:

#### Surgery

The goal of surgery is to remove all the cancer cells. In planning the surgery, the healthcare team keeps in mind how the surgery will affect your or your child's daily life. The extent of surgery for osteosarcoma depends on several factors, such as the size of the cancer and where it is{73}.

#### Chemotherapy

Chemotherapy treats cancer with strong medicines. For osteosarcoma, chemotherapy often is used before surgery. It can shrink the cancer and make it easier to remove. After surgery, chemotherapy treatments might be used to kill any cancer cells that might remain{74}. For osteosarcoma that returns after surgery or spreads to other areas of the body, chemotherapy might help relieve pain and slow the growth of the cancer{75}.

### B. Radiation therapy

Radiation therapy treats cancer with powerful energy beams. The energy can come from X-rays, protons or other sources. During radiation therapy, you lie on a table while a machine moves around your body. The machine directs radiation to precise points on your body. Radiation is not often used to treat osteosarcoma. Radiation therapy might be suggested instead of surgery if surgery can't remove all the cancer{76}.

### C. Ewing Sarcoma

Children with Ewing sarcoma should have their treatment planned by a team of health care providers who are experts in treating cancer in children{77}.

Three types of treatment are used:

### 1. Chemotherapy

Systemic combination chemotherapy is part of the treatment for all patients with Ewing tumors. It is often the first treatment given and lasts for about 6 to 12 months. Chemotherapy is often given to shrink the tumor before surgery or radiation therapy and to kill any tumor cells that may have spread to other parts of the body .Treatment includes vincristine-doxorubicin-cyclophosphamide {78}.

### 2. Radiation therapy

Radiation therapy is a cancer treatment that uses high-energy x-rays or other types of radiation to kill cancer cells or keep them from growing {79}.

Radiation therapy is used when the tumor cannot be removed by surgery or when surgery to remove the tumor will affect important body functions or the way the child will look. It may be used to make the tumor smaller and decrease the amount of tissue that needs to be removed during surgery. It may also be used to treat any tumor that remains after surgery and tumors that have spread to other parts of the body {80}.

### 3. Surgery

Surgery is usually done to remove cancer that is left after chemotherapy or radiation therapy. When possible, the whole tumor is removed by surgery. Tissue and bone that are removed may be replaced with a graft, which uses tissue and bone taken from another part of the patient's body or a donor. Sometimes an implant, such as artificial bone, is used {81}.

After surgical intervention ,some patients may be given chemotherapy or radiation therapy to kill any cancer cells that are left. Treatment given after the surgery, to lower the risk that the cancer will come back, is called adjuvant therapy {82}.

## 6.3 New types of treatment are being tested in clinical trials

### 1.Targeted therapy

Targeted therapy uses drugs or other substances to block the action of specific enzymes, proteins, or other molecules involved in the growth and spread of cancer cells{83}.

### 2. Immunotherapy

Immunotherapy helps a person's immune system fight cancer. Types of immunotherapy include:

- CAR T-cell therapy: This treatment changes the patient's T cells (a type of immune system cell) so they will attack certain proteins on the surface of cancer cells. T cells are taken from the patient and special receptors are added to their surface in the laboratory. The changed cells are called chimeric antigen receptor (CAR) T cells. The CAR T cells are grown in the laboratory and given to the patient by infusion{84}.

## Chondrosarcoma Treatment Option

### Surgery

Surgery is the main treatment for most types of chondrosarcoma. It may be used for tumours that are newly diagnosed and tumours that come back (recur). The following types of surgery may be used.

A- Wide resection removes the bone tumour and a wide margin of normal bone and tissue around the tumour. This type of surgery is also called an en bloc resection. It is the most common type of surgery used for chondrosarcoma. It is used to treat a chondrosarcoma in the bones of the skull or spine, as well as in the arm, leg and pelvis {85}.

B- Curettage is a procedure where the surgeon scrapes out the tumour without removing any of the bone. This leaves a hole where the tumour was removed. After curettage, the surgeon may use cryosurgery or bone cement to kill any remaining cancer cells {86}.

C- Bone cement is a type of chemical called polymethyl methacrylate that may be used after curettage to fix the hole left in the bone. This special cement heats up as it hardens, so it kills remaining cancer cells. It may be used after curettage to treat some small, low-grade chondrosarcoma tumours {87}.

D- Amputation removes all or part of the arm or leg with the tumour. It may be done when the chondrosarcoma has grown into the nerves or blood vessels, or if the tumour is very big. Amputation may be done if the cancer comes back in the same area after limb-sparing surgery. Most people who have an amputation will use an artificial limb (prosthesis) after surgery {88}.

## 6.4 Radiation therapy

External beam radiation therapy may be used to treat chondrosarcoma that can't be removed with surgery. It may also be used to destroy any cancer cells left behind after a wide resection or limb-sparing surgery. Radiation therapy is also used for recurrent chondrosarcoma {89}.

## 6.5 Chemotherapy

Chemotherapy is not used for low-grade chondrosarcoma because it has not been shown to help improve survival.

Mesenchymal chondrosarcoma is an aggressive, high-grade type of chondrosarcoma. It may be treated with one of the following combinations of chemotherapy drugs:

- vincristine, doxorubicin and cyclophosphamide (Procytox), alternated with ifosfamide (Ifex) and etoposide (Vepesid)
- vincristine, doxorubicin, ifosfamide and dactinomycin (Cosmegen)If mesenchymal chondrosarcoma has already spread (metastasized) at the time of the diagnosis, the following drug combination may be used:vincristine, doxorubicin and cyclophosphamide {90}.

## 7. The effect of physical therapy on joint and bone diseases

Rehabilitation is necessary to improve people's ability to live, work, and learn as much as possible and to maximize their functionality and quality of life. The impact extends to the community, society, and the economy{91}. While rehabilitation is a comprehensive, multicomponent, and multidisciplinary intervention, the specific health condition and other determinants of the health system or resources available determine the minimum components required, which often include physical therapy{92}.

Physical therapist interventions are required when movement and function are threatened to develop, maintain, and reestablish movement and functional capacity under the consideration that functional movement is fundamental to health and an optimal quality of life {93} .Despite the knowledge of the benefits of rehabilitation and physical therapy, these services are under-used{94}.

Before the COVID-19 crisis, in 2017 the World Confederation for Physical Therapy (WCPT) launched a collaboration to develop initiatives to the global practice and regulations of digital physical therapy practice through a Joint WCPT/INPTRA digital physical therapy Practice Task Force (Task Force). This report published in 2019 defined digital practice as “a term used to describe health care services, support, and information provided remotely via digital communication and devices”. The purpose of this initiative was “to facilitate effective delivery of physical therapy services by improving access to care and information and managing health care resources.”{95} However, for several physical therapists who have never had contact with this terminology, it is important to be aware that different terms are used in this field. There is still no global well-accepted term or definition for digital physical therapy among the literature industry, policymakers, and stakeholder groups. The variety of technologies that encompass this term may include tele-education, telemedicine, telemonitoring, teleassistance, mobile health, among others, and each field has its subset of technologies and specificities{96}.

An expanding elderly population and people with disabilities pose considerable challenges to the current healthcare system. As a practical technology that integrates systems and services, assistive physical therapy devices are essential to

maintain or to improve an individual's functioning and independence, thus promoting their well-being. Given technological advancements, core components of self-powered sensors and optimized machine-learning algorithms will play innovative roles in providing assistive services for unmet global needs. In this Perspective, we provide an overview of the latest developments in machine-learning-aided assistive physical therapy devices based on emerging self-powered sensing systems and a discussion of the challenges and opportunities in this field {97}.

Both physical therapy and intraarticular injections of glucocorticoids have been shown to confer clinical benefit with respect to osteoarthritis of the knee. Whether the short-term and long-term effectiveness for relieving pain and improving physical function differ between these two therapies is uncertain{98}.

Psychologically informed physical therapy search terms combined “psychotherapy,” “psychologically informed,” “psychological based,” “cognitive behavioral,” “acceptance and commitment,” “mindfulness,” and “psychological strategies” with “rehabilitation,” “physical therapy,” and “physiotherapy.” For the purpose of this review of summarizing behavioral change interventions, studies investigating education interventions for pain as the primary treatment component were not considered for inclusion.{99}.

Multifactorial physical therapy modalities have been widely utilized in clinical practice and are believed to be effective for improving symptoms, sport performance, and self-reported function in individuals with KOA {100}. These modalities usually involve hot pack treatment, electric stimulation, ultrasound, and combinations of these {101}, and studies have found. these physical therapy modalities to be beneficial for relieving pain and enhancing activities of daily living {102,100}.

In recent years, laser therapy has been introduced as a physical therapy modality for treating musculoskeletal conditions and has gained popularity since no evident side effects have been reported after intervention {103}. Of all the laser therapies, high intensity laser therapy (HILT) is a relatively new type of electrotherapy modality {104}.

It is a powerful and painless physical modality that has demonstrated significant benefits in analgesic, anti-edema, and biostimulating effects {105} .

Research has suggested that during HILT, radiation from high intensity laser produces photo-chemical, photothermal, and photomechanical actions especially from neodymium-doped yttrium aluminum garnet (Nd: YAG) laser, which has been found to be powerful in penetrating into deep tissues {106} .

Therapeutic exercise and physical therapy modalities can relieve pain intensity and alleviate back disability for patients with low back pain{107}.Transcutaneous electrical nerve stimulation and infrared ray thermal therapy are common modalities that are frequently used for treatment of chronic low back pain.{108}

Among the numerous therapeutic exercises available, therapeutic aquatic exercise is often prescribed by physicians for chronic low back pain, and it is becoming increasingly popular for treatment of chronic low back pain{109}. Therapeutic aquatic exercise refers to water-based treatments or exercise. Water is an ideal environment for conducting an exercise program given its various properties, including buoyancy pressure, density, thermal capacity, and conductivity{110}.

Low back pain (LBP) is a common health problem worldwide. Nearly 80% of the global population experience LBP at least once during lifetime{111}.

Physical therapy modalities are the most common conservative methods used in the treatment of LBP. In general, these modalities are combined with exercise and hot and cold pack, and electrotherapy {112}.

Several physical therapy modalities have been investigated in LBP studies; however, there is no consensus regarding the number of sessions and optimal intervals. Study designs in these studies often include the evaluation of treatment responses and outcomes, available modalities, and accessibility to treatment.Although the effectiveness of physical therapy modalities in knee OA has been evaluated in many studies, there is a very limited number of studies in the literature discussing their effects on sleep quality in knee OA patients. In the present study, we, therefore, aimed to evaluate the effect of physical therapy modalities on pain, sleep, mental status, and QoL of patients with OA and to

investigate the possible relationship between sleep quality and pain, psychological status, and QoL of OA patients {113}.

Physical therapy modalities that passively treat FM have also been investigated. In a previous systematic review, six types of massage therapy (Swedish massage, connective tissue massage, manual lymphatic drainage, myofascial release, Shiatsu, and a combination of severe massage styles) applied one to five times a week, for 4 to 40 weeks of treatment, were investigated as a therapeutic resource for patients with FM . Myofascial release has been shown to be more effective than placebo for improving pain, fatigue, stiffness, anxiety, depression, and quality of life of individuals with FM (moderate level of evidence) 16. Eight of the ten included articles in the review compared different types of massage therapy among themselves (with no placebo group) and showed limited scientific evidence for effectiveness of the other types of massage therapy. In addition, Swedish massage appears to be contraindicated because of the lack of benefit to patients{114}.

Patients with peripheral facial paralysis (PFP) have some degree of recovery. The aim of this study was to evaluate prognostic factors and physical therapy modalities associated with functional recovery in patients with PFP. This is a cohort study with 33 patients. We collected the following variables of patients who underwent treatment at the rehabilitation center:age, sex, risk factors, affected side, degree of facial paralysis (House-Brackmann scale), start of rehabilitation, and therapy modality (kinesiotherapy only; kinesiotherapy with excitomotor electrotherapy; and kinesiotherapy with excitomotor electrotherapy and photobiomodulation therapy) The outcomes were: degree of facial movement (House-Brackmann) and face scale applied 90 days after treatment{115}.

### 7.1 A comparison of two manual physical therapy approaches and electrotherapy modalities for patients with knee osteoarthritis: A randomized three arm clinical trial:

A broad spectrum of physical therapy exercise programs provides symptom relief and functional benefit for patients with knee OA. Manual physical therapy, including tailored exercise programs provide relatively higher level benefit that persists to one year. It is currently unknown if there are important differences in

the effects of different manual physical therapy techniques for patients with knee OA and there are virtually no studies comparing manual physical therapy and electrotherapy modalities. The aim of the study was to compare long-term results between three treatment groups (mobilization with movements [MWMs], passive joint mobilization [PJM], and electrotherapy) to determine which treatment is most effective in patients with knee OA.

A single-blind randomized clinical trial with parallel design was conducted in patients with knee OA. Seventy-two consecutive patients (mean age  $56.11 \pm 6.80$  years) with bilateral knee OA were randomly assigned to one of three treatment groups: MWMs, PJM, and electrotherapy. All groups performed an exercise program and received 12 sessions. The primary outcome measures of the functional assessment were the Western Ontario and McMaster Universities Osteoarthritis index (WOMAC) and Aggregated Locomotor Function (ALF) test scores.

The secondary outcome measures were pain level, measured using a pressure algometer and a visual analogue scale (VAS), range of motion (ROM), measured using a digital goniometer, and muscle strength, evaluated with a handheld dynamometer. Patients were assessed before treatment, after treatment and after 1 year of follow-up. Patients receiving the manual physical therapy interventions consisting of either MWM or PJM demonstrated a greater decrease in VAS scores at rest, during functional activities, and during the night compared to those in the electrotherapy group from baseline to after the treatment ( $p < 0.05$ ). This improvement continued at the 1-year follow-up ( $p < 0.05$ ).

The MWMs and PJM groups also showed significantly improved WOMAC and ALF scores, knee ROM and quadriceps muscle strength compared to those in the electrotherapy group from baseline to 1-year follow-up ( $p < 0.05$ ). In the treatment of patients with knee OA, manual physical therapy consisting of either MWM or PJM provided superior benefit over electrotherapy in terms of pain level, knee ROM, quadriceps muscle strength, and functional level{116}.

## 7.2 Types of physical therapy for bone and joint diseases

### 7.2.1 Rheumatoid Arthritis

Rheumatoid arthritis (RA) is a chronic and progressive inflammatory process resulting in the destruction of articular and periarticular tissues and leading to the development of functional impairment, permanent deformities and disability. RA affects approximately 1% of the global population and is more common in women than men {117}.

Physical therapy (PT) intervention in relieving inflammation. The effect of physical therapy interventions in the form exercise resulted in increased concentrations of short chain fatty acids and butyrate-producing bacteria which assist in regulating anti-inflammatory phenotypes. Also, improvements in cardiorespiratory fitness were positively correlated with lower pro-inflammatory biomarkers {118}.

The methods of hydrotherapy, therapeutic massage, laser therapy and physical exercise showed their effectiveness in the health status of individuals with the pathology, but there was no consensus on the parameters of the methods {119}.

They were managed with physical therapy, including thermotherapy, electrotherapy, laser therapy, magnetic field therapy and light therapy. After treatment, all study patients showed pain reduction, improved well-being, reduced duration of morning joint stiffness, improved ranges of motion in the joints and a better quality of life. Physical therapy and rehabilitation constitute the main method of treatment of this disorder {117}.

Physical therapy treatment aims to reduce pain, improve joint range, correct movement patterns, strengthen weak structures, improve cardiovascular endurance, and improve patients' quality of life {120}.

### 7.2.2 Osteoporosis

Osteoporosis is a disease that is characterized by low bone mass, deterioration of bone tissue, and disruption of bone microarchitecture: it can lead to compromised bone strength and an increase in the risk of fractures. Osteoporosis is

the most common bone disease in humans, representing a major public health problem{121}.

Physiotherapists take an active role in reducing the risk of falls and fractures by maintaining muscle strength, increasing bone mineral density, and improving balance{122}.

Physical therapy interventions directed at improving movement and mobility are of particular importance because physical inactivity is a cause of low bone mass, osteoporosis, and increased fall risk {123}.

Additionally, physical therapy interventions such as high-intensity resistive exercise targeted at improving strength and slowing decline in BMD are critical for fragility fracture prevention and recovery {124}.

However, further guidance is required regarding appropriate, specific physical therapy examination criteria and interventions for osteoporosis across clinical settings {125}.

### 7.2.3 Bone cancer

Bone cancer is taken into consideration a critical health problem, and in lots of cases, it reasons affected person death. The X-ray, MRI or CT-scan image is utilized by medical doctors to become aware of bone cancer. The manual technique is time-ingesting and required knowledge in that field. Therefore, it's miles important to broaden an automatic device to categorize and become aware of the cancerous bone and the healthful bone. The texture of a cancer bone is one-of-a-kind as compared to a healthful bone with inside the affected region {126}.

Physical therapists often treat cancer patients. Cancer treatment includes chemotherapy, radiotherapy, and surgery, which are being continuously developed and thus increase survival of patients with each cancer diagnosis. More specifically, 5-year survival rates increase with each cancer diagnosis. Cancer patients have many problems including muscle weakness, pulmonary dysfunction, fatigue, and pain. In the end, patients with cancer tend to have a decline in activities of daily living (ADL) and quality of life (QOL). Additionally, cancer patients often have progressive disease, depression, and anxiety. Physical therapy often helps patients regain strength and physical function and improve their QOL

and independence of daily living that they may have lost due to cancer or its treatment. Physical therapy has an important role in increasing physical function of cancer patients, cancer survivors, and children with cancer. In the future, physical therapy may be progressively needed for management of cancer patients {127}.

## 7.3 Physical therapy devices

### 7.3.1 Transcutaneous Electrical Nerve Stimulation

Transcutaneous Electrical Nerve Stimulation (TENS) is a treatment technique defined as an electrical current delivered to the surface of the skin that activates nerves. It reduces pain through a combination of peripheral and central mechanisms on the nervous system, and is divided into low and high frequency. It is indicated for several conditions, such as myofascial, neuropathic and arthritic pain. It is contraindicated in patients who are pregnant, have epilepsy or have a pacemaker. Overall, there is mixed evidence for the efficacy of TENS in chronic pain conditions and therefore a need for larger, more robust studies to evaluate its efficacy {128}.

Surgical procedures are ever more complex. Day-case surgical loads are increasing and the length of hospital stays are reducing. Management of pain in perioperative settings remains a challenge. Expert panels recommend a multimodal approach which is often interpreted by medical practitioners as polypharmacy. There is variability in non-pharmacological interventions offered to patients, although transcutaneous electrical nerve stimulation (TENS) has been used since the 1970s. Recommendations from expert panels are inconsistent about the use of TENS in perioperative pain settings{129}.



### 7.3.2 Electric Massager Device

The purpose of this paper is to identifying the effect of the proposed device using electrical stimulation and massage on the variable (muscular lengthening). The one with the pre, intermediate, and post-test due to its suitability to the nature of the research problem and to achieve its purpose, and the data was processed using the statistical bag (SPSS), and through the results collected, it was concluded that stimulation and electrical massage had positive effects in restoring muscle lengthening as soon as possible, and then returning Injured players to the fields of play, where it contributed to the return of the injured posterior thigh muscles to the normal state, and the researchers recommended to be guided by the proposed device, which was designed to rehabilitate the other injured thigh muscles {130} .

Electrical muscle stimulation (EMS) is an alternative method for preventing deep-vein thrombosis (DVT) by contracting the lower leg muscles, and its effect has been demonstrated by the fact that the action increases both the peak velocity and the blood flow in the deep veins of the lower extremities {131}.



### 7.3.3 Infrared massage devices

Chronic low back pain (CLBP) significantly affects the well-being of older adults, leading to diminished quality of life and heightened stress. Existing treatments have limited effectiveness and potential side effects. This study aimed to explore an integrative approach, employing a combination of spinal thermal massage bed (STMB) and intermittent pneumatic calf compression, as an alternative strategy for managing CLBP, improving body posture, reducing stress, and enhancing quality of life{132}.

Near infrared spectroscopy (NIRS) is increasingly used as a local tissue oxygenation equipment and it fulfills the functions of an efficient local microcirculation and a concussion growth monitor. Using it in surgery, physiotherapy or rescue indicates a high interdisciplinary diagnostic potential, which could lead us to improve the quality of patients' lives. The aim of this study was to review literature related to the physiotherapy aspect of using near infrared spectroscopy and to the consideration given to the development of this method{133}.



#### 7.3.4 Ultrasound physical therapy

Loading is indispensable for the growth, development, and maintenance of joint tissues, including mandibular condylar cartilage, but excessive loading or reduced host adaptive capacity can considerably damage the temporomandibular joint (TMJ), leading to temporomandibular joint osteoarthritis (TMJ-OA). TMJ-OA, associated with other pathological conditions and aging processes, is a highly degenerative disease affecting the articular cartilage. Many treatment modalities for TMJ-OA have been developed. Traditional clinical treatment includes mainly nonsurgical options, such as occlusal splints. However, non-invasive therapy does not achieve joint tissue repair and regeneration. Growing evidence suggests that low-intensity pulsed ultrasound (LIPUS) accelerates bone fracture healing and regeneration, as well as having extraordinary effects in terms of soft tissue repair and regeneration {134}.

Treatments for joint pain and dysfunction focus on restoration of joint motion, improvement in pain and a return to the previous level of the patient's daily activity. Therapeutic ultrasound is a noninvasive modality widely utilized in the management of musculoskeletal disorders. The objective of this systematic review

was to evaluate the effectiveness of therapeutic ultrasound in the management of patients with knee, shoulder and hip pain {135}.



## 8. x-rays of joints and bones

### 8.1 X-rays

The X-rays for which we performed the segmentation process make part from a database of images of DICOM type. They have a resolution of 2492 x 1984 pixels. An example of Xray can be observed in Fig {136}.



Figure 1. Chest X-ray (DICOM image).

Bone fracture can occur due to a simple accident or different types of diseases. So, quick and accurate diagnosis can be crucial to the success of any prescribed treatment. In practice, doctors and radiologists rely mainly on X-ray images to determine whether a fracture has occurred and the precise nature of the fracture. Manual inspection or conventional system of X-rays for fracture detection is a tedious and time consuming process. Computer vision system can help to screen X-ray images for suspicious cases and alarm the doctors. Depending on the experts alone for such a critical matter has caused intolerable errors and hence, the idea of automatic diagnosis procedure has always been an appealing one{137}.

presented Leg Bone Fracture Detection in x-ray image with preprocessing, segmentation, fracture detection and classification algorithm. It contains information about canny edge detector produces perfect information from the bone image for segmentation {138}.

Radiologists can identify the pathological changes associated with OA by analyzing highresolution knee X-ray images. Typically these changes cause the narrowing of joint space and development of bone spurs, leading to pain and impaired movement in patients. These pathologies are diagnosed in patients with developed Symptoms such as joint pain . However at early stages small pathological changes in bone microstructure can be evaluated by using a high-resolution technology such as MRI which is costly and not widely accessible{139} Those changes which take place in bone, whereby its condition is altered from one of health to disease, are accompanied by variations in opacity to x-rays. a decrease in density due to absorption of mineral matter is a much earlier and more quickly visible change than increase of density caused by extra deposition of mineral matter or new bony growth .Certain pathological conditions in bone are of course manifested by alteration of contour when examined by the X-rays, but even these are usually accompanied by changes in the opacity of the bony substance. It is therefore mainly to changes in density that one must look for help in the diagnosis of disease in bone {140}.

X-ray images (or Radiographs) are among the most common ways to detect problems in bones as well as other organs of the human body. The output image is a shadow-like image. Although CT and MRI images give better quality images for body organs than x-ray images, the latter are faster cheaper, enjoy wider availability and are easier to use with few limitations {141}.



## 8.2 Effects of X-rays on bone

In human bone the first clinical evidence of radiation damage is usually a loss in density, as seen in the roentgenograms. This may be generalized, with little alteration in texture, or it may be patchy, areas of very low density alternating with other areas which appear nearly normal. Islands of greatly increased density sometimes appear. They resemble those seen in caisson disease and are probably caused in both cases by necrosis of bone tissue distal to points of obliteration of nutrient vessels. Spontaneous fractures are common in irradiated bones, usually occurring from 8 months to 3 years after exposure. Nonunion is common, but many such fractures heal satisfactorily. A very serious, but fortunately rare, late effect of radiation is the induction of osteogenic sarcoma. If this is due to internally deposited radioactive isotopes rather than to external irradiation, malignant change is likely to be preceded by considerable abnormal bone proliferation in regions which, earlier, had seemed quite atrophic { 142 }.

The results of animal experimentation and of clinical observation indicate that both the anabolic and the catabolic processes in bone are damaged by external irradiation. Similar effects are produced by internally deposited radioactive isotopes.

## References

- 1- White, T. D., & Folkens, P. A. (2005). *The human bone manual*. Elsevier.
- 2- Steele, D. Gentry; Claud A. Bramblett (1988). *The Anatomy and Biology of the Human Skeleton*. Texas A&M University Press. 4. ISBN:0-89096-300-2.
- 3- Schmidt-Nielsen, Knut (1984). "Scaling: Why Is Animal Size So Important?". Cambridge: Cambridge University Press: 6. ISBN:0-521-31987-0.
- 4- . *Mammal anatomy : an illustrated guide*. New York: Marshall Cavendish. 2010.. 129 ISBN:9780761478829.
- 5- Hall John (2011). *Textbook of Medical Physiology* (. 12th). Philadelphia: Elsevier.. 957–960 ISBN:978-08089-2400-5.
- 6- Barnes-Svarney Patricia L.; Svarney Thomas E. (2016). *The Handy Anatomy Answer Book : Includes Physiology*. Visible Ink Press. 90–91. ISBN:978157859542.
- 7- 7. Currey, J. D. (2003). The many adaptations of bone. *Journal of biomechanics*, 36(10), 1487-1495.
- 8- Clarke, B. (2008). Normal bone anatomy and physiology. *Clinical journal of the American Society of Nephrology: CJASN*, 3(Suppl 3), S131.
- 9- Shier, David, Jackie Butler, and Ricki Lewis. "Chapter 7 Skeletal System." *Hole's Human Anatomy & Physiology*. 11th ed.
- 10- Brookes, M., Revell, W. J., Brookes, M., & Revell, W. J. (1998). Blood supply of flat bones. *Blood Supply of Bone: Scientific Aspects*, 64-74.
- 11- Yeung, A. Y., & Garg, R. (2022). *Anatomy, Sesamoid Bones*. In StatPearls [Internet]. StatPearls Publishing.
- 12- Cope PJ, Ourradi K, Li Y, Sharif M. Models of osteoarthritis: the good, the bad and the promising. *Osteoarthritis Cartilage*. 2019 Feb;27(2):230-239.
- 13- Tu C, He J, Wu B, Wang W, Li Z. An extensive review regarding the adipokines in the pathogenesis and progression of osteoarthritis. *Cytokine*. 2019 Jan;113:1-12.

- 14- Zang, J., Lu, L., & Yaszemski, M. J. (2017). Bone Disorders. In *Materials for Bone Disorders* (pp. 83-118). Academic Press.
- 15- Conforti, A.; di Cola, I.; Pavlych, V.; Ruscitti, P.; Berardicurti, O.; Ursini, F.; Giacomelli, R.; Cipriani, P. Beyond the joints, the extra-articular manifestations in rheumatoid arthritis. *Autoimmun. Rev.* 2021, 20, 102735. [Google Scholar] [CrossRef]
- 16- Cojocaru, M.; Cojocaru, I.M.; Silosi, I.; Vrabie, C.D.; Tanasescu, R. Extra-articular manifestations in rheumatoid arthritis. *Mædica* 2010, 5, 286–291. [Google Scholar] [PubMed]
- 17- Joseph, A.; Brasington, R.; Kahl, L.; Ranganathan, P.; Cheng, T.P.; Atkinson, J. Immunologic rheumatic disorders. *J. Allergy Clin. Immunol.* 2010, 125, S204–S215. [Google Scholar] [CrossRef].
- 18- Kurowska, W.; Kuca-Warnawin, E.H.; Radzikowska, A.; Maśliński, W. The role of anti-citrullinated protein antibodies (ACPA) in the pathogenesis of rheumatoid arthritis. *Cent. J. Immunol.* 2017, 42, 390–398. [Google Scholar] [CrossRef]
- 19- Wegner, N.; Lundberg, K.; Kinloch, A.; Fisher, B.; Malmström, V.; Feldmann, M.; Venables, P.J. Autoimmunity to specific citrullinated proteins gives the first clues to the etiology of rheumatoid arthritis. *Immunol. Rev.* 2010, 233, 34–54. [Google Scholar] [CrossRef]
- 20- Chaurasia, N.; Singh, A.; Singh, I.L.; Singh, T.; Tiwari, T. Cognitive dysfunction in patients of rheumatoid arthritis. *J. Fam. Med. Prim. Care* 2020, 9, 2219–2225. [Google Scholar] [CrossRef]
- 21- Lassere, M.N.; Rappo, J.; Portek, I.J.; Sturgess, A.; Edmonds, J.P. How many life years are lost in patients with rheumatoid arthritis? Secular cause-specific and all-cause mortality in rheumatoid arthritis, and their predictors in a long-term Australian cohort study. *Intern. Med. J.* 2013, 43, 66–72. [Google Scholar] [CrossRef] [PubMed]
- 22- Guo, Q.; Wang, Y.; Xu, D.; Nossent, J.; Pavlos, N.J.; Xu, J. Rheumatoid arthritis: Pathological mechanisms and modern pharmacologic therapies. *Bone Res.* 2018, 6, 1–15. [Google Scholar] [CrossRef] [PubMed]
- 23- Singh, J.A.; Saag, K.G.; Bridges, S.L.; Akl, E.A.; Bannuru, R.R.; Sullivan, M.C.; Vaysbrot, E.; McNaughton, C.; Osani, M.; Shmerling,

- R.H.; et al. 2015 American college of rheumatology guideline for the treatment of rheumatoid arthritis. *Arthritis Rheumatol.* 2016, 68, 1–26. [Google Scholar] [CrossRef]
- 24- Moura, M.D.G.; Lopes, L.C.; Silva, M.T.; Barberato-Filho, S.; Motta, R.H.L.; Bergamaschi, C.C. Use of steroid and nonsteroidal anti-inflammatories in the treatment of rheumatoid arthritis: Systematic review protocol. *Medicine* 2018, 97, e12658. [Google Scholar] [CrossRef].
- 25- Radu, A. F., & Bungau, S. G. (2021). Management of rheumatoid arthritis: an overview. *Cells*, 10(11), 2857.
- 26- NIH Consensus Development Panel on Osteoporosis Prevention, Diagnosis, and Therapy. Osteoporosis prevention, diagnosis, and therapy. *JAMA.* 2001;285:785–95. [PubMed] [Google Scholar]
- 27- Cosman F, de Beur SJ, LeBoff MS, Lewiecki EM, Tanner B, Randall S, et al. Clinician’s guide to prevention and treatment of osteoporosis. *Osteoporos Int.* 2014;25:2359–81. <https://doi.org/10.1007/s00198-014-2794-2>. [PMC free article] [PubMed] [Google Scholar]
- 28- Riggs BL, Wahner HW, Seeman E, Offord KP, Dunn WL, Mazess RB, et al. Changes in bone mineral density of the proximal femur and spine with aging. Differences between the postmenopausal and senile osteoporosis syndromes. *J Clin Invest.* 1982;70:716–23. <https://doi.org/10.1172/JCI110667>. [PMC free article] [PubMed] [Google Scholar].
- 29- Cosman F, de Beur SJ, LeBoff MS, Lewiecki EM, Tanner B, Randall S, et al. Clinician’s guide to prevention and treatment of osteoporosis. *Osteoporos Int.* 2014;25:2359–81. <https://doi.org/10.1007/s00198-014-2794-2>. [PMC free article] [PubMed] [Google Scholar].
- 30- Hannan MT, Felson DT, Dawson-Hughes B, Tucker KL, Cupples LA, Wilson PW, et al. Risk factors for longitudinal bone loss in elderly men and women: the Framingham Osteoporosis Study. *J Bone Miner Res.* 2000;15:710–20. <https://doi.org/10.1359/jbmr.2000.15.4.710>. [PubMed] [Google Scholar].

- 31- Qaseem A, Forcica MA, McLean RM, Denberg TD. ; Clinical Guidelines Committee of the American College of Physicians. Treatment of low bone density or osteoporosis to prevent fractures in men and women: a clinical practice guideline update from the American College of Physicians. *Ann Intern Med* 2017; 166 (11) 818-839.
- 32- Kuo TR, Chen CH. Bone biomarker for the clinical assessment of osteoporosis: recent developments and future perspectives. *Biomark Res* 2017; 5: 18.
- 33- Akkawi, I., & Zmerly, H. (2018). Osteoporosis: current concepts. *Joints*, 6(2), 122.
- 34- M. D. Blackledge, D. J. Collins, N. Tunariu et al., “Assessment of treatment response by total tumor volume and global apparent diffusion coefficient using diffusion-weighted MRI in patients with metastatic bone disease: a feasibility study,” *PLoS One*, vol. 9, no. 4, article e91779, pp. 1–10, 2014. View at: [Publisher Site](#) | [Google Scholar](#).
- 35- O. Bandyopadhyay, A. Biswas, and B. B. Bhattacharya, “Bone-cancer assessment and destruction pattern analysis in long-bone X-ray image,” *Journal of Digital Imaging*, vol. 32, no. 2, pp. 300–313, 2019. View at: [Publisher Site](#) | [Google Scholar](#).
- 36- Sharma, A., Yadav, D. P., Garg, H., Kumar, M., Sharma, B., & Koundal, D. (2021). Bone cancer detection using feature extraction based machine learning model. *Computational and Mathematical Methods in Medicine*, 2021.
- 37- Boulehmi, H., Mahersia, H., & Hamrouni, K. (2018, March). Bone cancer diagnosis using GGD analysis. In *2018 15th International Multi-Conference on Systems, Signals & Devices (SSD)* (pp. 246-251). IEEE.
- 38- Ferguson, J. L., & Turner, S. P. (2018). Bone cancer: diagnosis and treatment principles. *American family physician*, 98(4), 205-213.
- 39- Forlino, A.; Marini, J.C. Osteogenesis imperfecta. *Lancet* 2016, 387, 1657–1671. [[Google Scholar](#)] [[CrossRef](#)]
- 40- Götherström, C.; Westgren, M.; Shaw, S.S.; Åström, E.; Biswas, A.; Byers, P.H.; Mattar, C.N.; Graham, G.E.; Taslimi, J.; Ewald, U.;

- et al. Pre- and postnatal transplantation of fetal mesenchymal stem cells in osteogenesis imperfecta: A two-center experience. *Stem Cells Transl. Med.* 2013, 3, 255–264. [Google Scholar] [CrossRef]
- 41- Sillence, O.D.; Senn, A.; Danks, D.M. Genetic heterogeneity in osteogenesis imperfecta. *J. Med Genet.* 1979, 16, 101–116. [Google Scholar] [CrossRef] [PubMed] [Green Version]
- 42- Bregou, B.; Aubry-Rozier, B.; Bonafé, L.; Laurent-Applegate, L.; Pioletti, D.; Zambelli, P. Osteogenesis imperfecta: From diagnosis and multidisciplinary treatment to future perspectives. *Swiss Med. Wkly.* 2016, 146, w14322. [Google Scholar] [CrossRef]
- 43- Marini, J.C.; Forlino, A.; Cabral, W.A.; Barnes, A.M.; Antonio, J.D.S.; Milgrom, S.; Hyland, J.C.; Körkkö, J.; Prockop, D.J.; De Paepe, A.; et al. Consortium for osteogenesis imperfecta mutations in the helical domain of type I collagen: Regions rich in lethal mutations align with collagen binding sites for integrins and proteoglycans. *Hum. Mutat.* 2007, 28, 209–221. [Google Scholar] [CrossRef]
- 44- Rauch, F.; Lalic, L.; Roughley, P.; Glorieux, F.H. Relationship Between Genotype and Skeletal Phenotype in Children and Adolescents with Osteogenesis Imperfecta. *J. Bone Miner. Res.* 2009, 25, 1367–1374. [Google Scholar] [CrossRef] [PubMed] [Green Version]
- 45- Barnes, A.M.; Chang, W.; Morello, R.; Cabral, W.A.; Weis, M.; Eyre, D.R.; Leikin, S.; Makareeva, E.; Kuznetsova, N.; Uveges, T.E.; et al. Deficiency of Cartilage-Associated Protein in Recessive Lethal Osteogenesis Imperfecta. *N. Engl. J. Med.* 2006, 355, 2757–2764. [Google Scholar] [CrossRef] [PubMed] [Green Version]
- 46- Deguchi, M., Tsuji, S., Katsura, D., Kasahara, K., Kimura, F., & Murakami, T. (2021). Current overview of osteogenesis imperfecta. *Medicina*, 57(5), 464.
- 47- Ahmadi, H., Gholamzadeh, M., Shahmoradi, L., Nilashi, M., & Rashvand, P. (2018). Diseases diagnosis using fuzzy logic methods: A systematic and meta-analysis review. *Computer Methods and Programs in Biomedicine*, 161, 145-172.

- 48- Thawrani, D. P., Agabegi, S. S., & Asghar, F. (2019). Diagnosing sacroiliac joint pain. *JAAOS-Journal of the American Academy of Orthopaedic Surgeons*, 27(3), 85-93.
- 49- Palazzo, C.; Nguyen, C.; Lefevre-Colau, M.M.; Rannou, F.; Poiraudau, S. Risk factors and burden of osteoarthritis. *Ann. Phys. Rehabil. Med.* 2016, 59, 134–138.
- 50- Murphy, C.A.; Garg, A.K.; Silva-Correia, J.; Reis, R.L.; Oliveira, J.M.; Collins, M.N. The Meniscus in Normal and Osteoarthritic Tissues: Facing the Structure Property Challenges and Current Treatment Trends. *Annu. Rev. Biomed. Eng.* 2019, 21, 495–521.
- 51- Elsadek, B.E.M.; Abdelghany, A.A.; Abd El-Aziz, M.A.; Madkor, H.R.; Abd Elrady Ahmed, A.; Abd-Elghaffar, S.K.; Elsadek, A.A.M. Validation of the Diagnostic and Prognostic Values of ADAMTS5 and FSTL1 in Osteoarthritis Rat Model. *Cartilage* 2019, 1947603519852405
- 52- Fritz, B., & Fritz, J. (2022). Artificial intelligence for MRI diagnosis of joints: a scoping review of the current state-of-the-art of deep learning-based approaches. *Skeletal Radiology*, 51(2), 315-329.
- 53- Sukhonthamarn, K., Tan, T. L., Xu, C., Kuo, F. C., Lee, M. S., Citak, M., ... & Parvizi, J. (2020). Determining diagnostic thresholds for acute postoperative periprosthetic joint infection. *JBJS*, 102(23), 2043-2048.
- 54- Jerban, S., Chang, E. Y., & Du, J. (2020). Magnetic resonance imaging (MRI) studies of knee joint under mechanical loading. *Magnetic resonance imaging*, 65, 27-36.
- 55- Tournis, S., & Dede, A. D. (2018). Osteogenesis imperfecta—a clinical update. *Metabolism*, 80, 27-37.
- 56- Deane, K. D., & Holers, V. M. (2021). Rheumatoid arthritis pathogenesis, prediction, and prevention: an emerging paradigm shift. *Arthritis & Rheumatology*, 73(2), 181-193.
- 57- Forsyth, C., Kouvari, M., D’Cunha, N. M., Georgousopoulou, E. N., Panagiotakos, D. B., Mellor, D. D., ... & Naumovski, N. (2018). The effects of the Mediterranean diet on rheumatoid arthritis prevention and treatment: a systematic review of human prospective studies. *Rheumatology international*, 38(5), 737-747.

- 58- Semb, A. G., Ikdahl, E., Wibetoe, G., Crowson, C., & Rollefstad, S. (2020). Atherosclerotic cardiovascular disease prevention in rheumatoid arthritis. *Nature Reviews Rheumatology*, 16(7), 361-379.
- 59- Nguyen, V. H. (2017). Osteoporosis prevention and osteoporosis exercise in community-based public health programs. *Osteoporosis and sarcopenia*, 3(1), 18-31.
- 60- Manson, J. E., Cook, N. R., Lee, I. M., Christen, W., Bassuk, S. S., Mora, S., ... & Buring, J. E. (2019). Vitamin D supplements and prevention of cancer and cardiovascular disease. *New England Journal of Medicine*, 380(1), 33-44.
- 61- Nijhuis, W., Verhoef, M., van Bergen, C., Weinans, H., & Sakkars, R. (2022). Fractures in osteogenesis imperfecta: pathogenesis, treatment, rehabilitation and prevention. *Children*, 9(2), 268.
- 62- Palomo, T., Vilaça, T., & Lazaretti-Castro, M. (2017). Osteogenesis imperfecta: diagnosis and treatment. *Current Opinion in Endocrinology & Diabetes and Obesity*, 24(6), 381-388.
- 63- Ralston, S. H., & Gaston, M. S. (2020). Management of osteogenesis imperfecta. *Frontiers in endocrinology*, 10, 924.
- 64- Romão VC, Santos MJ, Polido-Pereira J, Duarte C, Nero P, Miguel C, et al. Comparative effectiveness of tocilizumab and TNF inhibitors in rheumatoid arthritis patients: Data from the Rheumatic Diseases Portuguese Register, Reuma.pt. *Biomed Res Int*. 2015;2015.
- 65- Smolen JS, Landewé RBM, Bergstra SA, Kerschbaumer A, Sepriano A, Aletaha D, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2022 update. *Ann Rheum Dis*. 2022 Nov 10;82(1):3–18.
- 66- Comparison of the efficacy of the tumour necrosis factor.
- 67- König MF, Grzes KM, Robinson PC, Pearce EJ. Sulfasalazine: a risk factor for severe COVID-19? Vol. 4, *The Lancet Rheumatology*. Elsevier Ltd; 2022. p. e388–9.
- 68- *The Lancet Rheumatology*. Exercise over analgesics for osteoarthritis in the UK. Vol. 4, *The Lancet Rheumatology*. Elsevier Ltd; 2022. p. e375.

- 69- Hua C, Buttgereit F, Combe B. Glucocorticoids in rheumatoid arthritis: Current status and future studies. Vol. 6, RMD Open. BMJ Publishing Group; 2020.
- 70- Wolkorte R, Heesink L, Kip MMA, Koffijberg H, Tabak M, Grünloh C. Monitoring of rheumatoid arthritis: a patient survey on disease insight and possible added value of an innovative inflammation monitoring device. *Rheumatol Int.* 2022 Sep 1;42(9):1565–72
- 71- Fries JF, Spitz P, Kraines RG, Holman HR. Measurement of patient outcome in arthritis. *Arthritis Rheum* 1980;23:137-45
- 72- Luqmani R , Hennell S, Estrach C, Birrell F, Bosworth A, Davenport G, et al. British Society for Rheumatology and British Health Professionals in Rheumatology guideline for the management of rheumatoid arthritis (the first 2 years). *Rheumatology* 2006;45:1167-9.
- 73- Lee M, George D, Khor S, Elvey M, Rashid A. Surgical Intervention for Rheumatoid Arthritis and Complication Risks. In: *Handbook of Systemic Autoimmune Diseases*. Elsevier Ltd; 2018. p. 127–60.
- 74- National Institute for Health and Clinical Excellence. Abatacept for the treatment of rheumatoid arthritis . (Technical appraisal 141). London: NICE, 2008. [www.nice.org.uk/ Guidance/TA141](http://www.nice.org.uk/Guidance/TA141)
- 75- National Institute for Health and Clinical Excellence. Osteoarthritis: the care and management of osteoarthritis in adults . (Clinical guideline 59). London: NICE, 2008.
- 76- Luqmani R, Hennell S, Estrach C, Basher D, Birrell F, Bosworth A, et al. British Society for Rheumatology and British Health Professionals in Rheumatology guideline for the management of rheumatoid arthritis (after the first two years). *Rheumatology* (advance access 27 Jan 2009; doi:10.1093/rheumatology/ken450
- 77- Lee JK, Choi CH. Total knee arthroplasty in rheumatoid arthritis. Vol. 24, *Knee Surgery and Related Research*. BioMed Central Ltd; 2012.
- 78- Riggi N, Suvà ML, Stamenkovic I. Ewing’s Sarcoma. Longo DL, editor. *New England Journal of Medicine* [Internet]. 2021 Jan

14;384(2):154–64.

Available

from:

<http://www.nejm.org/doi/10.1056/NEJMra2028910>

- 79- Womer RB, West DC, Krailo MD, Dickman PS, Pawel BR, Grier HE, et al. Randomized controlled trial of interval-compressed chemotherapy for the treatment of localized ewing sarcoma: A report from the children’s oncology group. *Journal of Clinical Oncology*. 2012 Nov 20;30(33):4148–54.
- 80- Heesen P, Ranft A, Bhadri V, En Edicte Brichard B, Collaud S, Cyprova S, et al. Value of adjuvant radiotherapy in patients with localized Ewing sarcoma at the extremities: Report from the Ewing 2008 trial. 2022.
- 81- Khan A, Sarkar E. CRISPR/Cas9 encouraged CAR-T cell immunotherapy reporting efficient and safe clinical results towards cancer. Vol. 33, *Cancer Treatment and Research Communications*. Elsevier Ltd; 2022.
- 82- Tamrazi A, Sundaresan S, Parvizi A, Eller A, Fujii J, Shaheen Z, et al. Clinical value of CT-guided biopsy of small ( $\leq 1.5$  cm) suspicious lung nodules: Diagnostic accuracy, molecular characterization and long-term clinical outcomes. *Cancer Treat Res Commun*. 2022 Jan 1;33.
- 83- Fromm J, Klein A, Baur-Melnyk A, Knösel T, Lindner L, Birkenmaier C, et al. Survival and prognostic factors in conventional G1 chondrosarcoma. *World J Surg Oncol*. 2019 Sep 3;17(1).
- 84- Liu S, Zhou X, Song A, Huo Z, Wang Y, Liu Y. Surgical treatment of chondrosarcoma of the sacrum with cement augmentation: A case report. *Medicine (United States)*. 2019;98(50).
- 85- A. Italiano OMAC. advance chondrosarcoma rol of chemotherapy and survival .
- 86- Scottish Intercollegiate Guidelines Network. Management of early rheumatoid arthritis (Guideline 48.) Edinburgh: SIGN, 2000. [www.sign.ac.uk](http://www.sign.ac.uk)
- 87- National Institute for Health and Clinical Excellence. Adalimumab, etanercept and infliximab for the treatment of rheumatoid arthritis . (Technical appraisal 130). London: NICE, 2007.

- 88- Fries JF, Spitz P, Kraines RG, Holman HR. Measurement of patient outcome in arthritis. *Arthritis Rheum* 1980;23:137-45
- 89- Al-Juwayr, B. J., & Al-Jumaily, A. S. (2014). Assessment of quality of life of osteoarthritis patients. *Ann Coll Med Mosul*, 40(1).
- 90- Berlinghieri, F. V. (1826). *Qawā'id al-uşūl aţ-ţibbīya* (Vol. 1). Maţba'at Būlāq.
- 91- World Health Organization. *World Report on Ageing and Health*. 2015. Accessed July 2020.
- 92- World Health Organization. *Rehabilitation in Health Systems*. 2017. Accessed July 2020.
- 93- World Confederation for Physical Therapy. *Policy statement: description of physical therapy*. 2017. Accessed June 2020.
- 94- Falvey JR, Murphy TE, Gill TM, Stevens-Lapsley JE, Ferrante LE. Home health rehabilitation utilization among Medicare beneficiaries following critical illness. *J Am Geriatr Soc*. 2020;68:1512–1519.
- 95- Dantas, L. O., Barreto, R. P. G., & Ferreira, C. H. J. (2020). Digital physical therapy in the COVID-19 pandemic. *Brazilian journal of physical therapy*, 24(5), 381.
- 96- COFFITO . 2020. Resolução No 516, de 20 de março de 2020 – Teleconsulta, Telemonitoramento e teleconsultoria. <https://www.coffito.gov.br/nsite/?p=15825>. Accessed 13.04.20
- 97- Xiao, X., Fang, Y., Xiao, X., Xu, J., & Chen, J. (2021). Machine-learning-aided self-powered assistive physical therapy devices. *ACS nano*, 15(12), 18633-18646.
- 98- Deyle, G. D., Allen, C. S., Allison, S. C., Gill, N. W., Hando, B. R., Petersen, E. J., ... & Rhon, D. I. (2020). Physical therapy versus glucocorticoid injection for osteoarthritis of the knee. *New England Journal of Medicine*, 382(15), 1420-1429.
- 99- Coronado, R. A., Brintz, C. E., McKernan, L. C., Master, H., Motzny, N., Silva, F. M., ... & Archer, K. R. (2020). Psychologically informed physical therapy for musculoskeletal pain: current approaches, implications, and future directions from recent randomized trials. *Pain reports*, 5(5).

- 100- Bennell KL, Buchbinder R, Hinman RS. Physical therapies in the management of osteoarthritis: current state of the evidence. *Curr Opin Rheumatol.* (2015) 27:304–11. doi: 10.1097/BOR.000000000000160
- 101- Bannuru RR, Osani MC, Vaysbrot EE, Arden NK, Bennell K, Bierma-Zeinstra SMA, et al. OARSI guidelines for the non-surgical management of knee, hip, and polyarticular osteoarthritis. *Osteoarthr Cartil.* (2019) 27:1578–89. doi: 10.1016/j.joca.2019.06.011
- 102- Woods B, Manca A, Weatherly H, Saramago P, Sideris E, Giannopoulou C, et al. Cost-effectiveness of adjunct non-pharmacological interventions for osteoarthritis of the knee. *PLoS One.* (2017) 12:e0172749. doi: 10.1371/journal.pone.0172749
- 103- Jang H, Lee H. Meta-analysis of pain relief effects by laser irradiation on joint areas. *Photomed Laser Surg.* (2012) 30:405–17. doi: 10.1089/pho.2012.3240
- 104- Wyszynska J, Bal-Bochenska M. Efficacy of high-intensity laser therapy in treating knee osteoarthritis: a first systematic review. *Photomed Laser Surg.* (2018) 36:343–53. doi: 10.1089/pho.2017.4425
- 105- Dundar U, Turkmen U, Toktas H, Solak O, Ulasli AM. Effect of high-intensity laser therapy in the management of myofascial pain syndrome of the trapezius: a double-blind, placebo-controlled study. *Lasers Med Sci.* (2015) 30:325–32. doi: 10.1007/s10103-014-1671-8
- 106- Venosa M, Romanini E, Padua R, Cerciello S. Comparison of high-intensity laser therapy and combination of ultrasound treatment and transcutaneous nerve stimulation in patients with cervical spondylosis: a randomized controlled trial. *Lasers Med Sci.* (2019) 34:947–53. doi: 10.1007/s10103-018-2682-7
- 107- Miyamoto GC, Franco KFM, van Dongen JM, et al. Different doses of Pilates-based exercise therapy for chronic low back pain: a randomised controlled trial with economic evaluation. *Br J Sports Med.* 2018;52(13):859-868.
- 108- Jamison RN, Wan L, Edwards RR, Mei A, Ross EL. Outcome of a high-frequency transcutaneous electrical nerve stimulator (hfTENS) device for low back pain: a randomized controlled trial. *Pain Pract.* 2019;19(5):466-475. doi:10.1111/papr.12764

- 109- Zampogna B, Papalia R, Papalia GF, et al. The role of physical activity as conservative treatment for hip and knee osteoarthritis in older people: a systematic review and meta-analysis. *J Clin Med.* 2020;9(4):1167. doi:10.3390/jcm9041167
- 110- Lahart IM, Metsios GS. Chronic physiological effects of swim training interventions in non-elite swimmers: a systematic review and meta-analysis. *Sports Med.* 2018;48(2):337-359. doi:10.1007/s40279-017-0805-0
- 111- Almeida DC, Kraychete DC. Low back pain-a diagnostic approach. *Rev Dor SãoPaulo.* 2017;18:173–177.
- 112- Altınbilek, T., & Murat, S. (2020). A comparison of application frequency of physical therapy modalities in patients with chronic mechanical low back pain. *Turkish journal of physical medicine and rehabilitation*, 66(2), 201
- 113- Altaş, E. U., & Demirdal, Ü. (2020). The effect of physical therapy and rehabilitation modalities on sleep quality in patients with primary knee osteoarthritis: a single-blind, prospective, randomized-controlled study. *Turkish journal of physical medicine and rehabilitation*, 66(1), 73
- 114- Yuan SL, Matsutani LA, Marques AP: Effectiveness of different styles of massage therapy in fibromyalgia: A systematic review and meta-analysis. *Man Ther.* 2015;20(2):257–64. 10.1016/j.math.2014.09.003
- 115- Cappeli, A. J., Nunes, H. R. D. C., Gameiro, M. D. O. O., Bazan, R., & Luvizutto, G. J. (2020). Main prognostic factors and physical therapy modalities associated with functional recovery in patients with peripheral facial paralysis. *Fisioterapia e Pesquisa*, 27, 180-187.
- 116- Kaya Mutlu, E., Ercin, E., Razak Ozdincler, A., & Ones, N. (2018). A comparison of two manual physical therapy approaches and electrotherapy modalities for patients with knee osteoarthritis: A randomized three arm clinical trial. *Physiotherapy theory and practice*, 34(8), 600-612.
- 117- Kuliński, W., & Skuza, J. (2021). Physical Therapy in Rheumatoid Arthritis. *Acta Balneologica*, 164(2) .

- 118- Fincher, C. R., Muraca, K., Torres, D., & Raynes, E. A. (2020). The Influence of Physical Therapy on Microbiotic Dysbiosis in Patients with Rheumatoid Arthritis. *The FASEB Journal*, 34(S1), 1-1.
- 119- Pereira, L. P. S., & Maia, M. D. S. (2021). Main physical therapy approaches in the treatment of rheumatoid arthritis: A literature review.
- 120- Meghe, S., Chitale, N., Phansopkar, P., Joshi, A., & Chitale, N. V. (2022). Effectiveness of Early Physical Therapy Rehabilitation in Patient With Juvenile Rheumatoid Arthritis. *Cureus*, 14(10).
- 121- Sözen, T., Özışık, L., & Başaran, N. Ç. (2017). An overview and management of osteoporosis. *European journal of rheumatology*, 4(1), 46.
- 122- Sarı, M., Öztürk, D., Çelik, H. İ., Çelik, Ö. M., Ünver, B., & Bek, N. (2023). Osteoporosis Knowledge, Physical Activity Level, and Calcium Intake in Students of Physical Therapy and Rehabilitation and Nutrition and Dietetics Departments. *HEALTH SCIENCES*, 3(2).
- 123- Pratt M, Norris J, Lobelo F, Roux L, Wang G. The cost of physical inactivity: moving into the 21st century. *Br J Sports Med*. 2014;48(3):171–173. doi:10.1136/bjsports-2012-091810
- 124- Avin, K. G., Nithman, R. W., Osborne, R., Betz, S. R., Lindsey, C., & Hartley, G. W. (2022). Essential components of physical therapist management of patients with osteoporosis: a Delphi study. *Journal of Geriatric Physical Therapy*, 45(2), E120-E126.
- 125- American Physical Therapy Association. *APTA Clinical Practice Guideline Process Manual, Revised*. American Physical Therapy Association; 2020. Accessed January 20, 202.
- 126- Ponlatha, D., Aravindhan, P., & Boovesh, L. (2022). Deep learning based classification of bone tumors using image segmentation. *Periodico di Mineralogia*, 3, 91-311.
- 127- Morishita, S., & Tsubaki, A. (2017). Physical therapy in patients with cancer. *Clinical physical therapy*, 95-120.
- 128- Aiyer, R., Johnson, E., & Poli, J. (2022). Transcutaneous electrical nerve stimulation. In *Anesthesiology In-Training Exam Review: Regional Anesthesia and Chronic Pain* (pp. 347-350). Cham: Springer International Publishing.

- 129- Johnson, M. I. (2017). Transcutaneous electrical nerve stimulation (TENS) as an adjunct for pain management in perioperative settings: a critical review. *Expert review of neurotherapeutics*, 17(10), 1013-1027.
- 130- Karam Salam Ismaeil, D. B. R. J., & Kadhim, H. A. A. (2023). The effect of using electrical stimulation and massage within a suggested device to restore muscle lengthening for athletes with a moderate-intensity muscle tear in some posterior thigh muscles. *Pakistan Heart Journal*, 56(1), 262-267
- 131- Sakai, M., Otsuka, T., Sugimura, K., Nishizawa, Y., Nagai, A., Yamamoto, S., ... & Kuroiwa, M. (2021). Use of electrical muscle stimulation body massager (EMS-BMs) improves deep venous blood flow. *Medical Engineering & Physics*, 92, 110-114.
- 132- Fajardo, J. C. S., Oh, S., Kim, B., Kim, S., Jang, G., & Yoon, B. (2023). Pain Reduction and Posture Alignment Improvement in Older Adults with Chronic Low Back Pain: A Novel Approach Using Spinal Thermal Massage Bed and Calf Pneumatic Cell Compression. *Medical Science Monitor: International Medical Journal of Experimental and Clinical Research*, 29, e940944-1.
- 133- Chroboczek, M., Jabłonska, A., Kubiak, R., Kujach, S., Luszczyk, M., & Laskowski, R. (2017). Usage of near infrared spectroscopy in physiotherapy. *Baltic Journal of Health and Physical Activity*, 9(3), 14.
- 134- Tanaka, E., Liu, Y., Xia, L., Ogasawara, N., Sakamaki, T., Kano, F., ... Yamamoto, A. (2020). Effectiveness of low-intensity pulsed ultrasound on osteoarthritis of the temporomandibular joint: a review. *Annals of biomedical engineering*, 48, 2158-2170.
- 135- Aiyer, R., Noori, S. A., Chang, K. V., Jung, B., Rasheed, A., Bansal, N., ... & Gulati, A. (2020). Therapeutic ultrasound for chronic pain management in joints: a systematic review. *Pain Medicine*, 21(7), 1437-1448.
- 136- Cosmin Cernazanu-Glavan, Stefan Holban, Segmentation of bone structure in X-ray images using convolutional neural network, Polytechnic University of Timisoara, Timisoara, Romania, 2013.p:2
- 137- - Ismail Hmeidi, Mahmoud Al-Ayyoub and Haya Rababah, Detecting Hand Bone Fractures in X-Ray

- 138- S. Myint, A. S. Khaing and H. M. Tun, “Detecting Leg Bone Fracture in X-ray Images”, International Journal of Scientific & Research, vol. 5, Jun. 2016, pp. 140-144.**
- 139- Livija Jakaite, Vitaly Schetin, Jiří Hladůvka, Sergey Minaev, Aziz Ambia & Wojtek**
- 140- Krzanowski Scientific Reports volume 11, Article number: 2294 (2021)**
- 141- Disease in bone and its detection by the X-rays EWH Shenton - 1911 - books.google.com**
- 142- American Cancer Society. Imaging (radiology) tests, 2013. <http://www.cancer.org/acs/groups/cid/documents/webcontent/003177pdf.pdf>[Online; accessed June-2013].**