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# BONE TISSUE REPAIRING BY HYDROGELS USING RADIATION METHOD

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## 1.Abstract

In this study, For the bone tissue engineering using gamma ray irradiation treatment using composition of the hydrogels in bone tissue repairing treatment.Hydrogel was studied using scanning electron microscopy(SEM) and energy dispersive X-ray spectroscopy (EDX) .The crystal structure of the silk fibroin (SF) composite hydrogels was confirmed with X-ray diffraction (XRD).[4] Bones provide mechanical protection for the body (such as protecting internal organs and blood forming marrow), facilitate locomotion, and serve As a supply source for the calcium, magnesium and phosphate minerals. Osteogenesis often requires a for replacement graft to restore the function of damaged tissue. Bone tissue engineering offer a promising alternative treatment for medical use, in addition to a controllable system for studies of biological function, development of biology and pathogenesis.

Bone tissue repair has garnered significant attention in regenerative medicine.[28] Hydrogels are becoming promising options for bone repair because they are biocompatible with the body, versatile, and can imitate the natural structure that supports cells. This review focuses on recent advances in using Radiation methods Facilitate precise regulation of hydrogel properties, which can be crucial for bone tissue engineering, highlighting key methodologies and the challenges. Radiation techniques including γ radiation, electron beam and UV radiation are employed to cross link polymer chains, thereby enhancing the mechanical properties and stability of hydrogels.[28] Challenges and feature directions in the fields are highlighted, emphasizing the need for optimizing radiation parameters and hydrogel formulations to achieve better clinical outcomes. This review provides a comprehensive overview of the state- of – the- art radiation method in hydrogel development and their implications for advancing bone tissue repair technologies.

## 2.Keywords

Hydrogels, Biocompatibility, Radiation cross-linking, Bone tissue repairing, Electron beam, Scaffold, Irradiation

## 3.Introduction

Significant health problems arise due to Bone abnormalities caused by tumors, diseases, infections, biochemical disorder, trauma and abnormal skeleton development.[2] Bone tissue engineering has significant advancement in recent years, driven by the need for effective strategies to repair and regenerate damage bone tissues. Hydrogels, three dimensional Webs of water-attracting polymers capable of retaining substantial amounts of water, have emerged as a versatile solution in this field. Their inherent properties, such as high biocompatibility tunable mechanical characteristics, along with the capability to support cell growth make them ideal candidate for bone tissue application. Bones provide mechanical protection to the body, facility locomotion, and they as a supply source for for calcium, magnesium and phosphate minerals. Numerous research efforts have addressed the development of an ideal scaffold for bone tissue engineering; however, they still have several limitations. For brain drug delivery and nerve regenerative engineering, polysaccharide base gels have been explored. Hydrogels have clear benefits over other bioactive materials when it comes to repairing bone tissue. they help stem cells stick, grow, and develop during the healing process. Hydrogels enable adhesion, proliferation and Stem cells' ability to differentiate during bone tissue repair.

Among various methods for hydrogel fabrication, radiation techniques have gained attention due to their ability to precisely control the cross-linking of polymer chains, radiation methods including gamma rays, electron beams and UV light, enable the creation of hydrogels with tailored properties Crucial for bone tissue development. this technique of several advantages such as uniform cross-linking, reduced reliance on chemical initiators, and enhanced control over the physical and chemical properties of hydrogels. This introduction explores the principles behind radiation- induced hydrogel synthesis and modification, outlining how this method contributes to the development of advanced material for bone repair. This review intends to provide an understanding of the impact of radiation technique on hydrogel properties and their potential applications in regenerative medicines.

## 4. Utilizing Hydrogels in Bone Regeneration

**4.1. Compositions and Properties:** Hydrogels are three dimensional Networks of water-loving polymers capable of holding Substantial volumes of water. Key properties for bone repair include biocompatibility, mechanical strength, along with the capability to support cell growth and differentiation. Hydrogels consists of hydrophilic polymers that form a network through physical or chemical cross-linking. The unique ability of a material to increase in size and preserve water without dissolving is provided by the cross-linkage structure. Common polymers include natural polymers and synthetic polymers.[2]

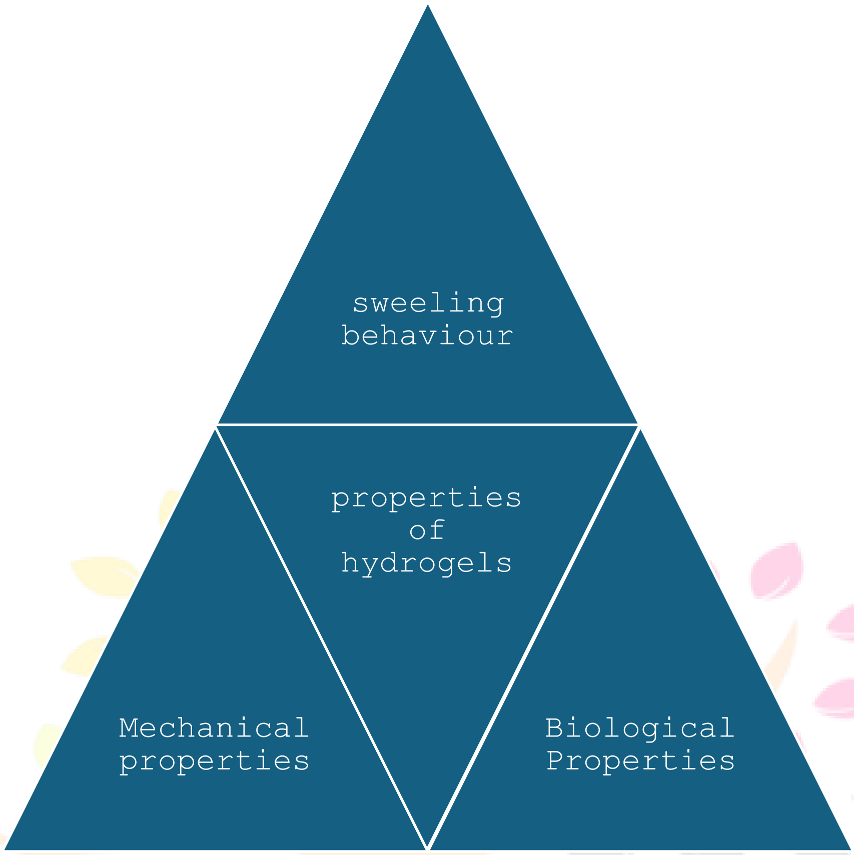


**Fig no.1.PROPERTIES OF HYDROGELS**

**4.1.1 Swelling Behavior:** The capacity of hydrogels to absorb water is essential for their functionality. Swelling happens because of the osmotic pressure difference between the inside of the hydrogel and the surrounding environment. This swelling property allows hydrogels to imitate extra cellular matrix, providing an ideal setting for cell growth and nutrient exchange.



**4.1.2 Mechanical Properties:** Hydrogels Can be modified to possess a range of mechanical properties by adjusting the polymer concentration, cross-linking density, and types of cross-linking agents. This flexibility is crucial in the field of bone tissue engineering because the hydrogels need to have the right balance of the load-bearing capacity and elasticity to match the demands of the bone tissue they are intended to repair.[29]

**4.1.3 Biocompatibility and Bioactivity:** For tissue engineering applications, hydrogels must be biocompatible, meaning they should not induce and adverse immune response. Moreover, the bioactivity of hydrogels can be improved by Strengthened through the integration of bioactive molecules, for example growth factors or inorganic materials. These additions help support the cellular activities needed for tissue regeneration.

4.1.4. **Radiations- Induced Cross-linking**: Radiation methods, like gamma rays, electron beams, and UV light, are used to cross- Connect the polymer chain in hydrogels. This process enhances their mechanical strength, stability, and degradation properties, making them more suitable for different biomedical applications. Additionally, these radiation techniques allow

Careful oversight of the for the properties of hydrogels, which is essential for customizing materials to meet specific needs in tissue engineering.

## 5.Types of Hydrogels

Common types are natural like collagen, alginate and synthetic like polyethylene glycol, polyvinyl alcohol, hydrogels. Each types have unique advantages in terms of degradation rates, mechanical properties, and biological interactions.[33]

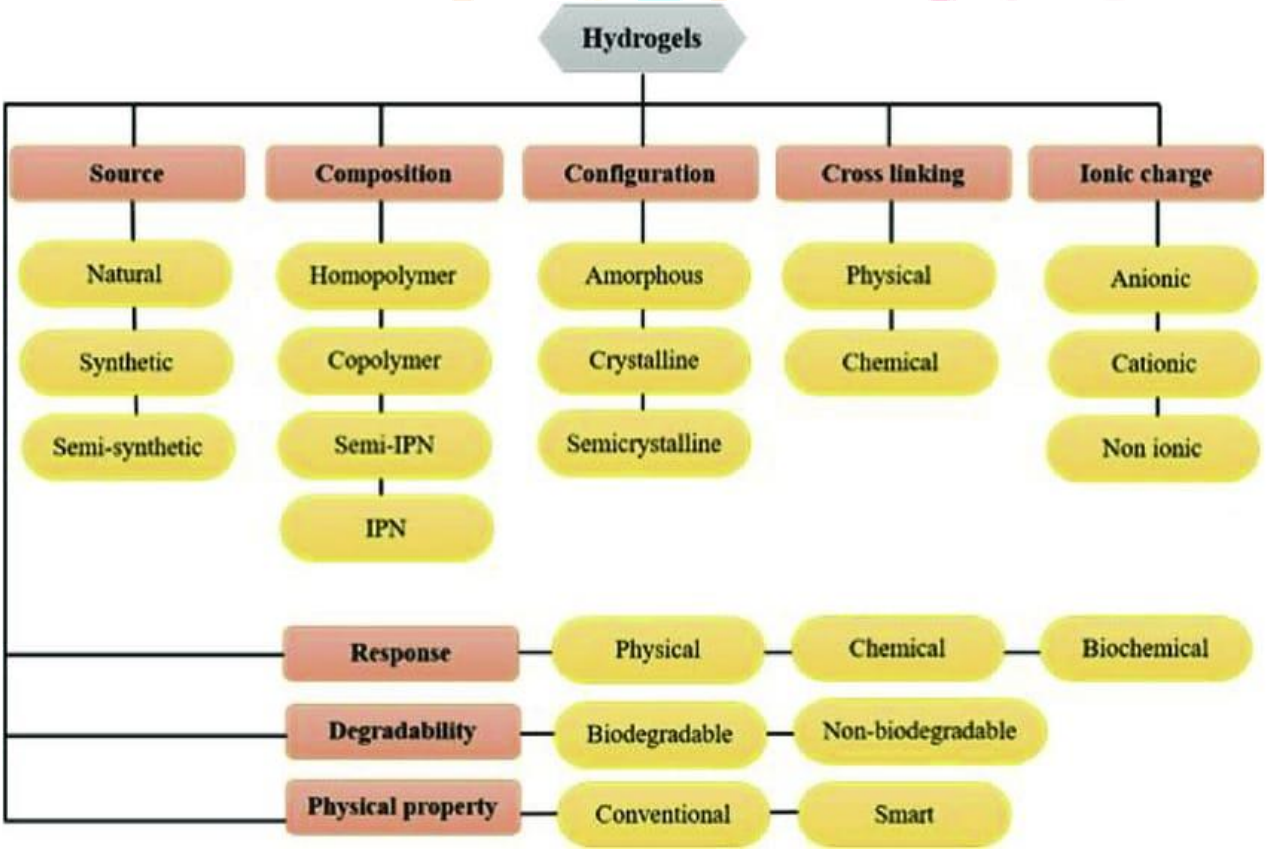


**Fig No.2 TYPES OF HYDROGELS**

The hydrogels classification depends on various types such as sources, composition, configuration, cross- linking, ionic charge, response, degradability, physical properties.

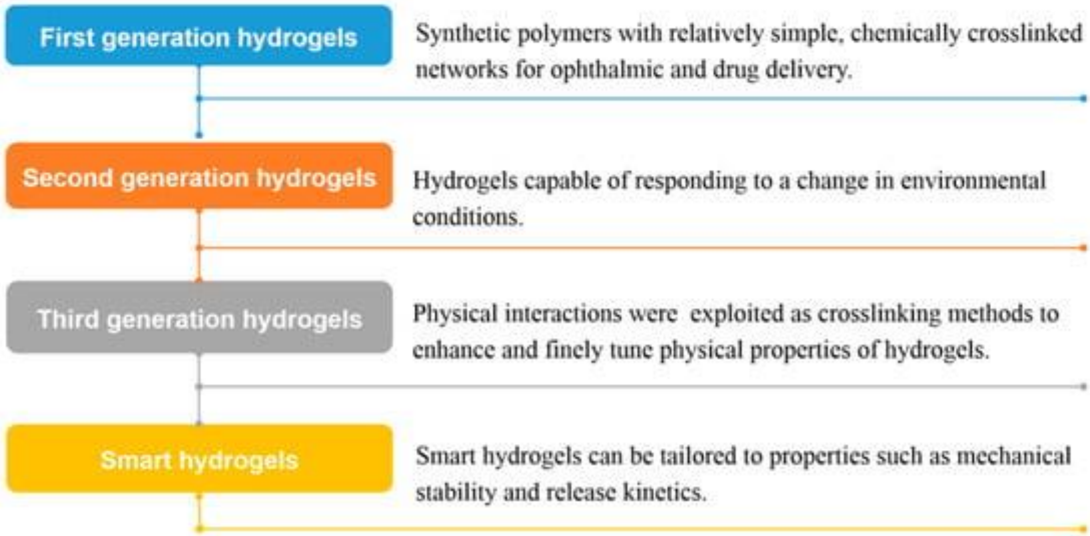


Fig No.3.TYPES OF HYDROGELS BY GENERATION

## 6.Radiation methods for hydrogel modification:

Radiation Techniques are pivotal in modifying hydrogels to enhance their properties for biomedical Practices, particularly related to tissue engineering.[31]to induce cross-linking these methods involve various forms of radiation. The new ionization Radiation method is use recently for hydrogels modification. Radiation methods are used to modify hydrogels in a variety of ways includes:

6.1. Radiations cross linking: In this Induces a Formation of cross-links between polymer chains in the method.

6.2. Radiations Polymerization: In this generates free radicals from monomers in the method.

6.3. Radiations Grafting. This method causes the polymer to produce radicals f graft Copolymerization.

Hydrogel fabrication with gamma radiation involves using intense gamma radiation to link together hydrophilic polymer chains. This process uses Isotopes including cobalt-60 to produce a stable, three-dimensional hydrogel from the initial solution.[31]

1.Gamma Radiation:

Process: Gamma rays, emitted from radioactive isotopes like Cobalt-60, penetrate the hydrogel and induce ionization of polymer chains.

Effects: This ionization leads to the formation of free radicals, which then initiate cross-linking reactions between polymer chains. Gamma radiation allows for uniform cross-linking throughout the hydrogel, improving its mechanical properties and stability.

Advantages: It offers high penetration depth, making it suitable for bulk hydrogel processing. Additionally, it requires no chemical initiators, minimizing potential cytotoxicity.

2.Electron Beam (E-beam) Radiation:

Process: High-energy electron beams are directed at the hydrogel, causing ionization and the creation of free radicals.

Effects: Similar gamma radiation, the free radicals facilitate cross-linking between polymer chains. E-beam radiation is acknowledged for its high efficiency and rapid processing times.

Advantages: It provides Careful regulation of the degree of cross-linking and is effective for high-throughput production. It also allows for deep penetration into thicker hydrogels.

3.Ultraviolet (UV) Radiation:

Process: UV light, typically from mercury lamps or LEDs, is used to irradiate hydrogels containing photo initiators.

Effects: Photo initiators absorb Ultraviolet light and produce free radicals, which initiate cross-linking in the fact of being present in suitable monomers. This method allows for the creation of hydrogels with specific patterns or shapes through mask-based techniques.

Advantages: UV radiation enables rapid and localized cross-linking, which is useful for fabricating hydrogels with complex geometries or surface modifications.

4.Combination Techniques:

Process: Combining different radiation methods, such as gamma and UV radiation, can further optimize hydrogel properties.

Effects: This approach can enhance cross-linking density, adjust swelling behaviour, and incorporate functional groups more effectively.

Advantages: It offers increased flexibility in tailoring hydrogel properties for specific applications.

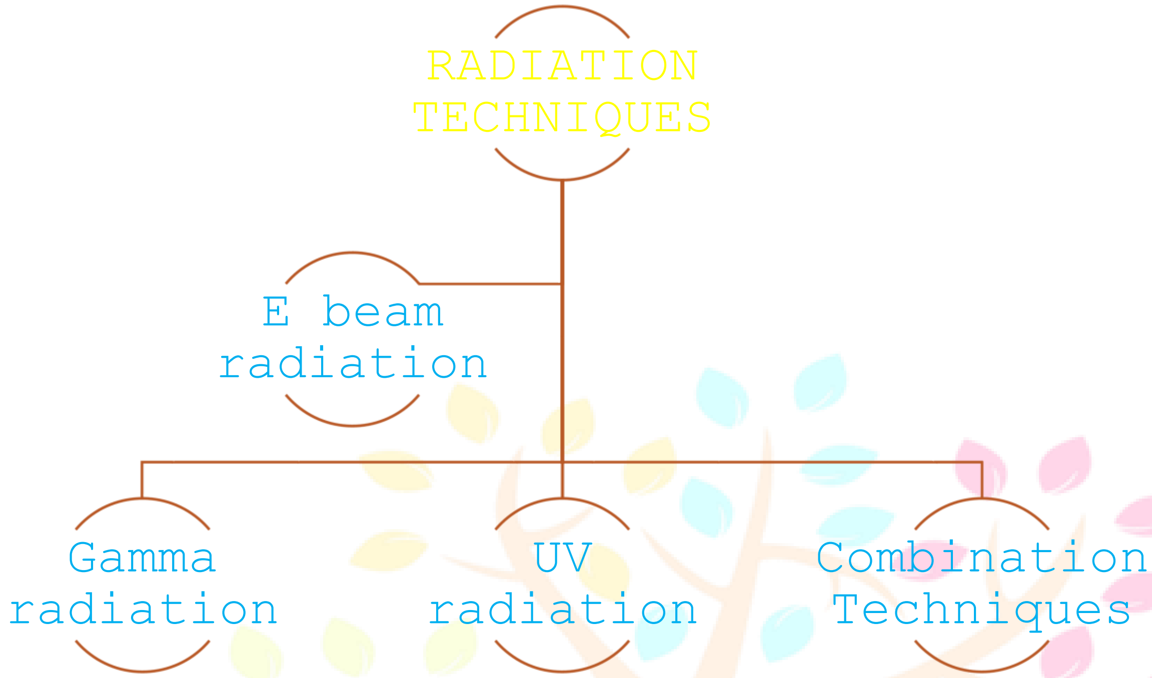


Fig No.4.RADIATION TECHNIQUES

Radiation method Can function to create hydrogels with specific properties for various applications. For example, gamma irradiation could be employed to create polyacrylic acid-co-polyacrylamide hydrogels, which can then be chemically adjusted to remove Metal ions from hazardous water.[31]

## 7.Applications Of Hydrogels in biological Tissue Engineering:

7.1. Enhances Mechanical Properties: Radiation-induced cross-linking improves the strength and elasticity of hydrogels, which is crucial for supporting and regenerating bone tissue.[30]

7.2. Controlled Degradation Rates: By adjusting radiation parameters, the losses its effectiveness over time of hydrogels can be fine-tuned as aligning the pace or level of similar resources or methods of bone healing. Incorporation of Bioactive Agents: Radiation methods facilitate the incorporation of bioactive molecules into hydrogels, promoting cell growth and bone formation. in summary, radiation methods provide a versatile and effective means of modifying hydrogels to meet the specific requirements of bone tissue engineering, offering benefits in terms of mechanical performance, stability, and bioactivity.

7.3. Scaffolds: Hydrogels can mimic extracellular matrices and provide structural integrity for cells to organize and grow.

7.4. cell encapsulation and delivery: The Hydrogel can encapsulate and deliver cells.

7.5. Tissue separations and bio-compatible adhesives: Hydrogels can Operate as tissue separations and bio-compatible adhesives.

7.6. Drug depots: Hydrogels can Act as storage sites for drugs.

7.7. Bioactive moiety delivery: Hydrogels can deliver bioactive moieties to encourage the natural reparative process.

7.8 Regenerating artificial cartilage: PVA hydrogels can be utilized to create artificial articular cartilage. Additionally, PVA hydrogels can facilitate the formation of bone-like apatite.

Bone-like apatite formation: PVA hydrogels can serve to form bone-like apatite.

7.9. Treating spinal cord injuries: Hydrogels can stabilize the inflammatory environment at the lesion site and provide a suitable environment for regeneration.

7.10. Restoring tissue damaged by brain injuries: Hydrogels may serve as a viable option for regenerating tissue lost due to brain injuries.

7.11 Hydrogels derived by the Extracellular Matrix: The extracellular matrix (ECM) of native tissues maintains their structural integrity by offering physical support. It acts as an adhesive surface for cell attachment and organization, while also serving as a supply source for biochemical signals that promote cell survival and differentiation.[15]

7.12. Photopolymerized hydrogels in tissue engineering:

It has been Use in an extensive range of Biomedical applications. in tissue engineering, Hydrogels have been utilized to modify and enhance tissue function, serving as tissue barriers. They have also been explored as materials for carrying cells in tissue replacement strategies.[15]

7.13. Bones Regeneration: Radiation-modified hydrogels can promote the attachment, growth, and development of osteoblasts, which boosts bone regeneration.

7.14. Delivery Systems: Radiation-modified hydrogels can act as carriers for growth factors, drugs, or genes that help promote bone healing.

7.15 Scaffold Integration: These Hydrogels are capable of integrated with other materials like ceramics or metals to improve their mechanical properties and suitability for load-bearing applications.

# 8.Advantages of Radiation Method:

## 8.1. Radiations-induced polymerization:

A Radiation -induced penetrating polymerization method can create hydrogels that combine the best feature of elastomers and hydrogels. these can have similar young's Modulus and friction values pertaining to human skin, and they can withstand better compression and puncture loads.[26]

## 8.2. Tissue Adhesion:

Hydrogels have good tissue adhesion and shape Adaptation, and this is excellent property of the hydrogels.[25]

## 8.3 Sterilization:

Efficiency: Radiation can effectively sterilize equipment and materials, killing bacteria, viruses, and other pathogens.

Penetration: It can penetrate through packaging and materials, making it suitable for sterilizing items that are difficult to clean with other methods.

No Residues: Unlike chemical sterilization, radiation does not leave harmful residues on products.

## 8.4. Imaging:

Detailed Images: In medical imaging (like X-rays and CT scans), radiation provides detailed internal images of the body, aiding in diagnosis and treatment planning.

Non-Invasive: Allows for internal examination Without the necessity for invasive interventions.

## 8.5. Therapy:

Targeted Treatment: In cancer treatment (radiotherapy), radiation can precisely target and destroy cancer cells while minimizing damage to surrounding healthy tissue.

Effective for Specific Types: Beneficial for categories of cancers and conditions that are less responsive to other treatments.

## 8.6. Industrial Applications:

Non-Destructive Testing: Radiation is used in non-destructive testing to inspect the integrity of materials and structures without damaging them.

## 8.7 Preservation:

Food Preservation: Radiation can enhance the preservation of food by killing spoilage organisms and pests.

Each application of radiation has its own specific advantages, but it's essential to manage and control radiation use carefully to minimize potential health risks and environmental impacts.

8.8Therapeutic reagent delivery:

Hydrogels can serve the role of as on demand it is intelligent delivery system to release therapeutic reagents.

8.9 Self-healing:

Hydrogels have the self -healing properties

8.10 Radioprotection:

Hydrogels can serve the role of shield tissues from radiation damage. For instance, they can be placed between the prostate and the rectum to deliver a higher radiation dose Towards the prostate during reducing the risk of injury to the rectum.[11]

8.11 Mechanical and biochemical properties:

Hydrogels have excellent mechanical and biochemical properties, including the antibacterial, antioxidant, and adhesive abilities.[25]

8.12 ECM-derived hydrogels:

Hydrogels derived from the supportive matrix outside the cells (ECM) can help repair injured tissues.

For example, can help with pulmonary damage and oedema after radiation exposure the lung ECM-derived hydrogels use.[12]

8.13 Platelet-rich hydrogels:

Platelet rich hydrogels can help protect against radiation -induced dermatitis and bone injury.

Precision and Control: Radiation allows for Meticulous control of the crosslinking density and network structure of hydrogels, leading to improved mechanical strength and stability.[13]

Reduced Chemical Usage: Unlike chemical crosslinking agents, radiation methods do not introduce potentially toxic residues into the hydrogel.

Customization: The extent and type of crosslinking can be adjusted to meet the specific requirements of different bone repair applications

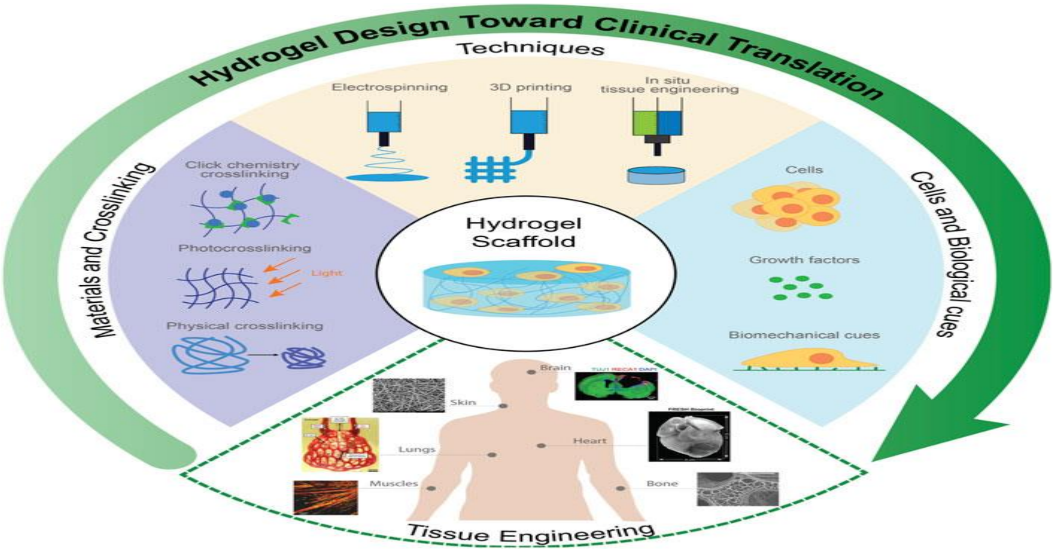


Fig No.5.ADVANTAGES OF TISSUE ENGINEERING

# 9.Prepared To aid in bone tissue healing using radiation:

## 9.1 Photo-cross-linking:

We developed A new Bone-regenerative peptide hydrogels has been developed using ultraviolet radiation. This hydrogel supports bone regeneration by promoting calcium salt deposition in osteoblasts and boosting the expression of genes associated with osteoblast function. [33]

## 9.2 Gamma or electron beam irradiation:

High-energy radiation can cross-link water-soluble polymer or monomer chain ends Without the requirement of a cross-linker. This method can be performed at room temperature and physiological pH, but the radiation can damage cells and tissues.

## 9.3 UV light irradiation:

Liquid hydrogels and BMSCs were co-cultured with Factor A and Factor B, and then cured with UV light irradiation. This hydrogel mixture was used to fill osteochondral defect areas in layers.

## 9.4 Sol-gel method:

This method was used to prepare a thermosensitive chitosan-based hydrogel reinforced with nano hydroxy apatite.[33]

### 9.5 3D printing:

This microfabrication technique can create 3D structures with the desired architecture or shape.[33]

## 10.Challenges and Future Directions:

### 10.1Challenges:

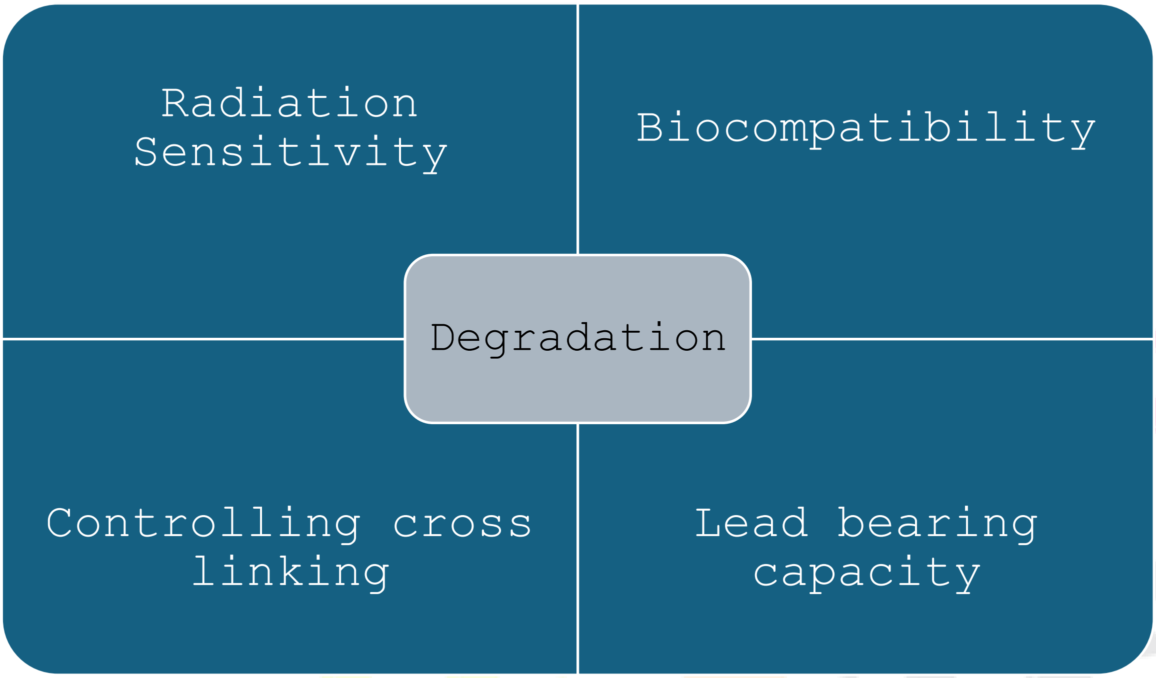


Fig No.6.CHALLENGES OF HYDROGELS BY RADIATION METHOD

10.1.1 Radiation Sensitivity: Hydrogels can be sensitive to radiation, which can alter the own physical and chemical properties, Potentially Affecting their performance in bone repair.

10.1.2 Biocompatibility: Ensuring the Hydrogels remain biocompatible after radiation-induced modifications is crucial. could Compromise their effectiveness by unwanted side effects or toxicity.

10.1.3 Controlled Cross-linking: Getting Detailed command of the cross-linking density of hydrogels through radiation is difficult, but it's essential for ensuring they have the physical characteristics of needed for effective bone repair.[26]

10.1.4 Degradation: The degradation of hydrogels under physiological conditions can be difficult to control.

10.1.5 Lead bearing capacity: Hydrogels need to have adequate mechanical strength to support bone repair. Ensuring achieves the desired strength without compromising the hydrogels other properties is a significant challenge in radiation method.

## 10.2 Future Directions:

10.2.1 Advanced Radiation Techniques: Development of more precise and controlled radiation techniques could improve the cross-linking process and minimize unwanted changes in the hydrogel properties.

10.2.2 Hybrid Materials: Combining hydrogels with other materials or bioactive agents could enhance their performance. For instance, incorporating nanoparticles or growth factors might improve both their mechanical strength and biological functionality.

10.2.3 Customization and Optimization: Tailoring hydrogels for specific types of bone defects and repair requirements through radiation-induced modifications could lead to more effective treatments.

10.2.4 Long-term Studies: More research is needed on the long-term effects of radiation-processed hydrogels in biological systems, including their stability, degradation, and interaction with surrounding tissues.

10.2.5 Clinical Trials: Moving from laboratory research to clinical trials is vital for evaluating the real-world effectiveness and safety of radiation-processed hydrogels for bone regeneration.

10. 2.6 Biomimetic hydrogels: Mimicking the natural extracellular matrix of bone by incorporating similar protein components and mimicking its mechanical properties for better cell adhesion and differentiation.[28]

10.2.7. Multi-functional hydrogel: Integrating bioactive factors such as growth factors, osteoconductive molecules, or small-molecule drugs into hydrogel matrices can significantly enhance targeted stimulation of bone formation. This approach leverages the unique properties of hydrogels—such as biocompatibility, flexibility, and the ability to replicate the natural extracellular environment making them ideal for bone tissue engineering.

**Key Strategies for Integration:**

1. **Growth Factors**: Incorporating bone morphogenetic proteins (BMPs) or VEGF into hydrogels can promote osteogenesis and angiogenesis. Controlled release systems can be created to have deliver these factors over time, optimizing the bone healing process.

2. **Osteoconductive Molecules**: Using osteoconductive materials like hydroxyapatite or collagen can enhance the scaffolding properties of hydrogels. These materials create a favourable environment for cells attachment and proliferation, facilitating bone regeneration.

3. **Small-Molecule Drugs**: Integrating drugs that influence cellular pathways related to bone formation, such as bisphosphonates or RANKL inhibitors, can modulate local cellular responses. This targeted approach can improve the overall efficacy of bone repair.

**Benefits of Hydrogel Integration:**

- **Customization**: The mechanical and biochemical properties of hydrogels can be adapted to suit the specific needs of the target tissue.
- **Biodegradability**: Hydrogels can be engineered to break down in synchrony with tissue regeneration, minimizing the need for surgical removal.
- **Cellular Interaction**: The permeable framework of hydrogels facilitates nutrient diffusion and provides a scaffold for cellular migration and proliferation.

**Applications in Bone Regeneration:**

1. **Bone Defect Healing**: Hydrogels loaded with bioactive factors can be used in critical-sized bone defects to promote new bone formation and healing.
2. **Osteoporosis Treatment**: Delivering drugs or growth factors via hydrogels can help stimulate bone density in osteoporotic patients.
3. **Maxillofacial Surgery**: Hydrogel systems can be employed to restore bone in complex craniofacial defects, where precise targeting of bioactive factors is crucial. [28]

10.2.8 Responsive hydrogels: Designing hydrogels that can change their properties based on environmental cues like pH or temperature, allowing for Targeted delivery of bioactive substances at the injury site.[28]

These advancements could significantly enhance the utility of hydrogels in regenerative medicine, offering better solutions for bone repair and regeneration.

10.2.6 Long-term Stability: Ensuring that the hydrogels maintain their properties over extended periods and in physiological conditions is crucial for clinical applications.

10.2.7 Regulatory and Safety Aspects: Addressing regulatory concerns and ensuring the safety of radiation-modified hydrogels in clinical settings are important for their successful translation to the clinic.

# 11.Conclusion:

Radiation methods present a powerful approach to enhancing the properties of hydrogels for bone tissue engineering. By allowing precise control over crosslinking and reducing the need for chemical additives, these techniques hold great promise for creating effective and safe materials for bone repair. Ongoing research is needed to address current challenges and fully realize the potential of radiation-modified hydrogels in clinical application

# Benefits of Radiation-Crosslinked Hydrogels

1. Biocompatibility: Hydrogels created through radiation methods are typically biocompatible, making them suitable for use in medical applications without adverse reactions.

2. Controlled Degradation: The degradation rates of these hydrogels may be tailored, allowing them to match the natural healing processes in bone regeneration.

4. Mechanical Properties: Radiation-induced crosslinking provides fine-tuned control over the mechanical strength and porosity of the hydrogels, both of which are critical for supporting new bone growth.

5. Future Directions in Research

6. 1. Optimization of Radiation Parameters: Exploring various radiation doses and types can help refine the properties of hydrogels, making them more effective for specific applications.

2. Incorporation of Bioactive Agents: Adding growth factors or osteoconductive materials into the hydrogel matrix can enhance their functionality, promoting faster and more effective bone healing.

3. In Vivo Studies: Conducting extensive in vivo studies is crucial to assess the long-term efficacy and safety of radiation-modified hydrogels, providing insights into their performance in real biological environments.

Advancing research in radiation-modified hydrogels could lead to more personalized and effective treatments for bone repair and regeneration. By addressing current challenges and focusing on optimization, we can realize the complete capability of these innovative materials in clinical applications, ultimately improving patient outcomes in tissue engineering.

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