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THE IMPACT OF BIOLOGICAL THERAPIES ON CHONDRAL LESIONS
SUMMARY OF THE DOCTORAL THESIS

PhD Supervisor:
PROF. UNIV. DR. POPESCU GHEORGHE ION

PhD Student:
VIŞOIANU ANDREI

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Introduction

Chondral lesions represent a current topic, in a context where diagnostic methods are becoming increasingly advanced and frequently used, while the population's exposure to the factors that can cause them is continuously increasing. A meta-analysis on the incidence of chondral lesions showed that they are present in 60-66% of performed arthroscopies, with over 900,000 people in the USA being diagnosed with cartilage lesions. In Romania, a retrospective study conducted on 355 consecutive arthroscopies identified chondral lesions in 69.6% of cases. The progression of this condition, as mentioned earlier, leads to the development of osteoarthritis. The global number of osteoarthritis cases has significantly increased, with an estimated 528 million people in 2019, a 113% increase from 1990 .

Considering the multitude of therapeutic approaches and the variability in results of clinical studies, this thesis aimed to identify the most effective treatment methods for small chondral lesions and the early stages of osteoarthritis, focusing on improving both the symptoms and the functionality of the knee.

1. Demographic Data. Anatomy of Articular Cartilage. Definitions and Classifications. Causes. Diagnostic Methods.

Cartilage lesions can have multiple causes, including acute trauma, degenerative changes secondary to trauma, accumulation of repeated chronic microtraumas, acquired metabolic factors, or developmental anomalies, such as in the case of osteochondritis dissecans [2]. The symptoms may begin suddenly following a traumatic event or may develop progressively. The most common lesions are located at the level of the medial femoral condyle, which is the segment that bears the majority of the joint load.

The main complaints of affected individuals are pain and relative or sometimes total functional impairment. A first mandatory radiological evaluation consists of performing standard radiographs in various views: anteroposterior and lateral weight-bearing views, Rosenberg view (a radiograph taken in the anteroposterior direction with the knees flexed at 45°), and the "skyline view" radiograph.

Magnetic Resonance Imaging (MRI) is the most commonly used non-invasive method for evaluating cartilage. It allows for accurate diagnosis of morphological changes in articular cartilage, ranging from simple cracks to complete destruction of cartilage thickness. Although MRI examination has improved recently in terms of cartilage lesion evaluation, it has not been able to replace arthroscopic evaluation.

2. Therapeutic Approaches in Cartilage Lesions

Medication treatment includes, among other things, the administration of anti-inflammatory drugs with analgesic effects, commonly used in medical practice, such as acetaminophen, diclofenac, naproxen, loxoprofen sodium, ibuprofen, etc. These drugs inhibit the synthesis of COX-1 and COX-2, reducing the inflammatory process and alleviating pain, but they carry the risk of irritating the gastric mucosa. When used long-term, these drugs can lead to liver, kidney, or hematological disorders.

Hyaluronic Acid administration aims to restore the viscosity and elasticity of the synovial fluid, as well as regulate the osmolarity of the cartilage. At the same time, it improves the immune and inflammatory responses and supports the synthesis of proteoglycans. By administering hyaluronic acid, we improve shock absorption, joint mobility, and especially reduce pain and the local inflammatory process.

Another therapeutic option is the administration of Platelet-Rich Plasma (PRP). The principle behind PRP is to activate a cascade of regenerative biological processes, aimed at healing the tissues. PRP releases a concentration of growth factors and cytokines. PDGF (platelet-derived growth factor) released by platelets, endothelial cells, macrophages, or smooth muscle cells has a mitogenic effect on mesenchymal cells and osteoblasts; it regulates the secretion of collagenases and collagen synthesis; has a chemotactic effect on macrophages and neutrophils, and stimulates mitogenesis in fibroblasts. TGF (transforming growth factor) stimulates mesenchymal cell proliferation; regulates collagen synthesis and collagenase secretion; stimulates angiogenesis, and inhibits the proliferation of macrophages and lymphocytes. VEGF (vascular endothelial growth factor) contributes to increased angiogenesis and vascular permeability; at the same time, it stimulates mitogenesis for endothelial cells. IGF-I acts as a chemotactic factor for fibroblasts, stimulating protein synthesis; it also stimulates bone formation through the proliferation and differentiation of osteoblasts.

Another treatment alternative is BMAC (Bone Marrow Aspirate Concentrate), which is a source of mesenchymal stem cells. The number of platelets varies from one patient to another, lymphocytes account for 13%, eosinophils for 2.2%, and monocytes and basophils account for 1.3%, and 0.1%, respectively, of the total cellular composition. Adipose-derived stem cells (ADSC), although involving a simple and inexpensive procedure and increasingly used, have a lower chondrogenic differentiation capacity compared to BMAC.

One method of stimulating the bone marrow is by performing microfractures at the site of the lesion. This technique can be performed minimally invasively through arthroscopic surgery. It is a technique recommended for small-sized lesions, based on the principle that by performing these microfractures, a series of growth factors are released from the underlying bone, which will stimulate the formation of new fibrocartilage tissue designed to fill the defect. The fibrocartilage tissue obtained is mechanically and biologically different from the native hyaline cartilage, but it is capable of restoring joint function and alleviating pain.

3. Working Hypothesis and Main Objectives

The objective of this work is to identify optimal treatment methods for cartilage lesions and the early stages of osteoarthritis. By utilizing current biological treatments administered intra-articularly, we aim to restore joint homeostasis.

The main hypothesis we started with is that intra-articular administration of biological therapies leads to better functional outcomes and symptom reduction in patients with cartilage lesions, while promoting anti-inflammatory and regenerative processes.

4. Enhancement of Microfracture Treatment for Chondral Lesions through Platelet-Rich Plasma Administration

I conducted an observational study between October 2022 and October 2024, involving a group of 24 patients diagnosed with cartilage lesions in the knee. These patients were treated either with arthroscopic microfracture alone or with the same procedure combined with autologous platelet-rich plasma (PRP) injection, in order to assess the effectiveness of supplementing the treatment with PRP. To ensure homogeneity of the group and minimize the influence of other factors on the results, patient selection was based on strict criteria.

Included were patients aged 18 to 60, with cartilage lesions in the medial compartment of the knee, classified as grade 3 or 4 in the Outerbridge system, with lesion sizes ranging from 2–3 cm^2. All patients were monitored clinically and functionally at baseline, and then at 3 months, 6 months, and 12 months post-intervention, using the IKDC (International Knee Documentation Committee) and VAS (Visual Analogue Scale) scores.

The IKDC scores of patients in both groups showed improvements at the 3-month, 6-month, and 1-year evaluations. At all three time points (3 months, 6 months, and 1 year), patients in the group treated with microfracture combined with PRP injection had significantly higher IKDC scores compared to those in the group treated only with microfracture, indicating a more evident functional improvement following the combined treatment. The differences observed between the two groups were statistically significant at each time point analyzed ($p < 0.05$).

At all three evaluation points (3 months, 6 months, and 1 year), the group treated only with microfracture had significantly higher VAS scores than the group that received PRP. The differences between the two groups were statistically significant for each analyzed time period ($p < 0.05$). These results suggest that patients treated solely with microfracture experienced a higher level of residual pain throughout the three stages of the study, as a higher VAS score reflects a greater perception of pain.

In analyzing the relationship between age and IKDC score progression, there was no significant correlation between age and improvement in the IKDC score in the group that received microfracture and PRP. However, in the group treated only with microfracture, there was a tendency towards a moderate negative correlation, suggesting that older patients might experience less improvement, although this result was not statistically significant. The small sample size limits the robustness of the conclusions. A study with a larger sample size would be useful to confirm these trends.

5. Comparison of the Efficacy of Hyaluronic Acid and Platelet-Rich Plasma in Early Osteoarthritis

I conducted an observational study between August 2021 and March 2024, which included 32 patients diagnosed with mild symptomatic osteoarthritis. The classification of the patients was based on standard knee radiographs using the Kellgren and Lawrence system.

Functional evaluations of the patients were performed initially, at six months, and then at one year, using the Lysholm score.

To assess the symptoms, the VAS (Visual Analogue Scale) was used, with values ranging from 0 to 10, where 0 was considered the complete absence of pain, and 10 represented the maximum pain intensity.

The treatment was randomly allocated, with some patients receiving hyaluronic acid (HA), and others receiving platelet-rich plasma (PRP).

We can affirm that gender does not significantly influence the improvement in the Lysholm score at 6 months or 1 year, regardless of the treatment. Although there were minor average differences (e.g., women in the PRP group had a slightly higher score at 1 year), these differences were not statistically significant.

In the PRP group, there was a slight trend suggesting that older patients experienced greater improvement in the Lysholm score, but this relationship was not statistically significant. In the HA group, there was no clear relationship between age and the improvement in the Lysholm score. Statistical significance ($p > 0.05$) was absent in all cases, meaning age did not significantly influence the improvement in the Lysholm score in either group.

At 6 months, there were no significant differences between the PRP and HA treatments, suggesting that both treatments were effective in equal proportions in the short term. However, at 1 year, the PRP treatment led to a significantly greater improvement in the Lysholm score compared to HA, suggesting a stronger long-term effect of PRP. Thus, PRP may be more effective in the long term, but for similar results in the short term, both treatments appear comparable.

Descriptive analysis shows that at 6 months post-treatment, the HA group had a greater average decrease in the VAS score compared to the PRP group (−3.20 vs. −2.53), suggesting a more pronounced short-term pain reduction effect of hyaluronic acid. However, at 1 year post-intervention, the PRP treatment led to a more pronounced improvement in the VAS score (−4.35) compared to HA (−3.40), indicating a greater long-term effectiveness of PRP.

6. Applications of Biological Therapy in Other Musculoskeletal Conditions

Considering the effectiveness of biological therapies in the treatment of cartilage pathologies, as well as their well-documented anti-inflammatory and regenerative capacities in the specialized literature, I have extended the use of these treatments to other structures of the musculoskeletal system. The administration of PRP has shown notable benefits in alleviating myofascial pain, patellar tendinopathy, Achilles tendon disorders, as well as lateral epicondylitis, results that are discussed in more detail in the respective chapter.

7. Conclusions and Personal Contributions

The arthroscopic surgical technique involving microfracture can be enhanced by the administration of platelet-rich plasma (PRP). Using the IKDC score, it was observed that patients who received PRP achieved significantly higher scores compared to those who only underwent microfracture, at both 3 months, 6 months, and 1 year. This translates to better functionality following the adjunctive treatment. Regarding the pain scale, VAS values were consistently higher in patients treated solely with microfracture compared to those who received PRP. This reflects a much more pronounced reduction in pain for patients who received the biologic treatment with PRP.

PRP treatment demonstrated a greater and more consistent improvement in the Lysholm score compared to hyaluronic acid (HA) treatment in patients with early-stage osteoarthritis. This favorable trend for PRP is evident at 6 months and becomes even more pronounced at 1 year, while HA produces more modest and variable improvements, sometimes accompanied by decreases in the Lysholm score.

Although no significant differences were found at 6 months between the two treatments, suggesting comparable short-term efficacy, at 1 year, PRP resulted in a significantly greater improvement in the Lysholm score compared to HA, indicating a more durable therapeutic effect.

Although the differences observed in the VAS scale at both evaluation points (6 months and 1 year) were not statistically significant ($p > 0.05$), the described trends may indicate a differentiated therapeutic response over time: HA acts more quickly, while PRP develops its effect gradually but sustained. This aspect is important in treatment selection based on the patient's profile, the severity of the lesion, and clinical objectives – short-term pain reduction or long-term functional improvement.

Through this thesis, I have outlined a therapeutic approach for cartilage lesions and early stages of osteoarthritis based on real clinical results, and paved the way for further research into musculoskeletal pathologies.

I have demonstrated the long-term benefits of administering active biologic treatment in the form of PRP as an adjunct to surgical arthroscopic treatment with microfractures.

I have comparatively evaluated the administration of platelet-rich plasma versus hyaluronic acid in the treatment of early-stage osteoarthritis and demonstrated the advantages of biologic therapy in the long term.

I have expanded the applicability of PRP therapy to other musculoskeletal pathologies and presented the preliminary results obtained.

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LIST OF PUBLICATIONS RELATED TO THE DOCTORAL THESIS TOPIC

1. **Visoianu A**, Soare G, Baciu CC, Ene R, Popescu GI, *Enhancing Microfracture Treatment for Chondral Lesions with Platelet-Rich Plasma: an Observational Study*, Farmacia,2025,vol.73,no.2, FI-1,4/2024, Q4, pag.422–429, capitolul 4
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2. **Visoianu A,** Soare G, Ene R, Popescu GI, Baciu CC, and Rizea C, *Cold laser, hyaluronic acid, platelet-rich plasma: save the best for last in treating, early phases of ostheoarthritis*, Journal of Optoelectronics and Advanced Materials,2025, no. 3–4, vol. 27, pag. 176–183, FI-0.6/2023, Q4, capitolul 5
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3. **Visoianu A**, Soare G, Baciu CC, and Ene R, *Recurrent Achilles Tendon Rupture Following Open Surgical Repair, Treated Nonoperatively, and Enhanced With Biological Platelet- Rich Plasma (PRP) Therapy: A Case Report*, Cureus, 2025, capitolul 6,
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