

**PART 1: RESEARCH DETAILS & INSTITUTION CONTACT INFORMATION**

<b>Full Research Title:</b>	<b>Use of Hyaluronic Acid for Rotator Cuff Tendinopathy: Preliminary Results</b>
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## PART 2: RESEARCH PROPOSAL

**Purpose and Hypothesis:** The purpose of this study was to analyze the use of hyaluronic acid plus nicotinamide (HA-NAD) for the treatment of rotator cuff tendinopathy. We hypothesize that HA-NAD (Playal) is a safe and effective option.

**Aims and Objectives:** This study aimed to study the clinical results of HA-NAD in rotator cuff tendinopathy, using OXFORD and VAS scores.

### Unsolved Research Questions

The tendon healing process is slow and structured in multiple phases, from inflammatory cytokine recruitment to growth factors and reparative cell involvement. It is widely known that a result of the healing process is the frequent formation of inferior fibrotic scar tissue or fibrous adhesions, which modify the structure and function of the tendon. Beyond preventive measures, therapeutic strategies in case of chronic lesions include biomechanical corrections, anti-inflammatory drugs, instrumental therapies such as shock wave or electromagnetic field stimulation, and the administration of hyaluronic acid or biological factors, such as platelet-rich plasma (PRP) or growth factors (GFs). Surgery is still the treatment of choice for acute tendon lesions, choosing between tendon repair and reconstruction with different grafts and materials. The findings of some studies are that HA injections improve symptoms and function in patients with rotator cuff disorders, without side effects and reactions. NSAIDs administrations and cortisone injections, if prolonged, may be contraindicated in elderly patients with comorbidities<sup>1-3</sup> such as diabetes or hypertension. The HA is physiologically present in the synovial fluid<sup>4</sup>: its main role is to lubricate the joint, it exerts mechanical and biological functions, in terms of antiadhesive shock absorber and articular stabilizer against shear stresses<sup>5</sup>, and it presents some analgesic effects<sup>6</sup>. The HA is a polymer of disaccharides, composed by D-glucuronic acid and D-N-acetyl-glucosamine, synthesized by a class of integral membrane proteins. It is present in the extracellular matrix, and is a biomechanical and functional element of the articular cartilage<sup>7</sup>. Specifically, the HA is viscoelastic, lubricates and protects the articular surface and cartilage from stress and friction forces.<sup>8</sup> Four studies<sup>9,10-12</sup> comparing patients undergoing HA vs phosphate-buffered saline injections reported good clinical results and pain relief. In particular, Blaine<sup>10</sup> showed better ROM recovery, reduced pain at night, and significantly higher overall satisfaction in the HA group; Meloni<sup>9</sup> showed a significant difference in the improvement of clinical symptoms and recovery of functional status in patients at 1 month after the end of the HA infiltrative cycle, in particular HA group VAS score was 2.8 respect 8.0 in the sodium chloride solution group.

### Clinical Relevance

This minimally invasive procedure with HA-NAD (Playal) provides an optimized environment for regeneration and decrease pain. As very few studies have evaluated the results after HA to treat rotator cuff tendinopathies, this could settle the basis for understanding the clinical outcomes and possible advantages or disadvantages after this treatment option.

## **Materials and Methods**

### **Study Design**

30 patients (18 - 65) with rotator cuff tendinopathy, treated with one ultrasound-guided injection of H-NAD followed prospectively for 6 months. Comparative analysis of preoperative, and postoperative scores using patient-reported assessment instruments will be performed to examine clinical outcomes.

### **Inclusion Criteria:**

1. Patients with symptomatic rotator cuff tendinopathy for more than 3 months
2. Age between 18 to 65 years
3. Patients who consented to the treatment modality as per the protocol

### **Exclusion Criteria:**

1. Rheumatoid Arthritis
2. Corticosteroid injection in the last 3 months
3. Severe cardiovascular disease
4. Patients with blood diseases, systemic metabolic disorders, immunodeficiency, Hepatitis B or C, HIV positive status, local or systemic infection.
5. Positive Covid19-Test
6. Smokers

### **Ultrasound-guided Injection Technique**

The procedure was performed in a standardized way in the outpatients' office with the patient in the up right position using local disinfection, sterile drape, and marking the site of injection. A senior orthopaedic surgeon will inject all the shoulders using an ultrasound-guided approach. He first checked the tendon thickness and its superior limit. Subsequently, the subacromial space is injected with 2 cc (HA-NAD - 40 mg) using a specific syringe and a 22G needle.

### **Postoperative Protocol**

We will instruct the patients to do some simple exercises at home according to a standard protocol of physiotherapy<sup>13</sup> for 1 month.

**Clinical Testing:** OXFORD and VAS

**Study Design:** Prospective Clinical Study

**Expected Outcome:** Significant improvement in all clinical scores at 1, 3 and 6 months comparing with the pre-treatment state.

## Related Literature

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