

Adhesive Photocurable Hydrogels for Cartilage Repair: A Critical Translational Appraisal of Preclinical Evidence and Office-Based Feasibility

Frare Andre Luiz* and Iwassaki Rodrigo Dias

Department of Physiotherapy Research and Diagnosis of the SBED (Brazilian Society for the Study of Pain), Brazil

***Corresponding Author:** Frare Andre Luiz, Department of Physiotherapy Research and Diagnosis of the SBED (Brazilian Society for the Study of Pain), Brazil.

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Abstract

Adhesive hydrogels are being investigated as scaffolds capable of remaining within focal chondral defects while supporting cellular retention and matrix deposition. This narrative critical appraisal examines the preclinical evidence reported by Karami and colleagues for phosphoserine-functionalized, photocurable hydrogels and considers whether those findings justify office-based intra-articular use. The source study combined mechanical testing, implantation into surgically created caprine cartilage defects, histology, and *in-vitro* culture of bovine chondrocytes. Its results support local retention and tissue-interface integration after direct placement followed by 405-nm photopolymerization. They do not, however, establish efficacy after unguided or image-guided intra-articular injection, demonstrate clinical benefit in humans, or validate commercial products not chemically shown to be equivalent to the tested MePha and MePGa formulations. The evidence should therefore be interpreted as an early device-level proof of concept rather than as confirmation of a routine injectable treatment. Translation will require complete material characterization, dose and curing validation, biodistribution studies, standardized histological scoring, adequately powered animal comparisons, toxicology, and prospective human trials. Adhesive hydrogel technology is scientifically promising, but claims of superior clinical efficacy or practical in-office applicability remain premature.

Keywords: Adhesive Hydrogel; Cartilage Repair; Photopolymerization; Translational Medicine; Preclinical Evidence; Chondral Defect

Clinical problem and biological rationale

Articular cartilage heals poorly because it is avascular, has low cellular density, and depends on a highly organized extracellular matrix for load distribution. Focal lesions may progress symptomatically and structurally, yet no single intervention reliably restores native hyaline cartilage across all defect types. Marrow-stimulation procedures can generate repair tissue with fibrocartilaginous characteristics, whereas osteochondral transfer and autologous chondrocyte implantation are technically demanding and remain sensitive to defect size, fixation, cell retention, and integration at the border with native cartilage [2-6].

Hydrogels address part of this problem by providing a hydrated three-dimensional matrix that can carry cells or bioactive agents. Their value depends on more than viscosity. Relevant properties include polymer chemistry, cross-link density, curing kinetics, interfacial adhesion, degradation, swelling, cytocompatibility, and mechanical behavior under cyclic joint loading. A formulation that is injectable

but does not remain at the defect may disperse through the joint; one that adheres strongly but cures incompletely may expose tissue to residual reagents or light-dependent variability [7-11].

Evidence examined

The principal experimental evidence assessed here is the proof-of-concept report by Karami, *et al.* [1], together with its preceding description of intrinsically adhesive injectable photocurable hydrogel networks [12]. In the 2024 study, methacrylated phosphoserine-containing hyaluronic-acid and gelatin formulations (MePHa and MePGa) were cross-linked with a photoinitiator under 405-nm light. The investigation incorporated bench mechanical measurements, direct placement into full-thickness caprine cartilage defects, histological follow-up, and *in-vitro* encapsulation of bovine chondrocytes.

The distinction between the tested materials and any named commercial viscoelastic is essential. Numerical results from MePHa or MePGa cannot be transferred to another product unless composition, degree of functionalization, polymer concentration, photoinitiator, light dose, rheology, degradation, sterility, and manufacturing controls are demonstrated to be equivalent.

Mechanical and adhesive findings

Karami, *et al.* reported increasing adhesive and compressive performance with higher polymer content. At 15% polymer, the published compressive moduli were approximately 468.2 ± 44.2 kPa for MePHa and 264.9 ± 25.6 kPa for MePGa [1]. These values describe the specific experimental formulations and test conditions; they are not generic properties of hyaluronic-acid gels, platelet-rich plasma, fibrin preparations, or products marketed under different names.

Comparison with fibrin glue is useful as a laboratory benchmark, but it should not be presented as proof of superior patient outcomes. A higher modulus or tensile adhesion value does not by itself establish resistance to fatigue, preservation of cartilage congruity, absence of abrasive wear, or long-term biological safety. Joint loading is multiaxial and cyclic, and clinically relevant performance also depends on defect geometry, surface preparation, curing depth, synovial fluid, and rehabilitation.

In-vivo evidence

In the caprine model, the material was placed directly into a surgically created full-thickness defect and photopolymerized *in situ*. Histology suggested better continuity at the host-repair interface in treated defects than in empty controls, with Alcian blue staining used to examine glycosaminoglycan-rich matrix [1]. This is meaningful evidence of retention and interface behavior under the conditions tested.

Several limits constrain interpretation. The experiment was small and exploratory; the comparison was primarily descriptive; and the repair tissue did not unequivocally reproduce mature native hyaline cartilage. Empty-defect controls do not answer whether the hydrogel is superior to microfracture, osteochondral transfer, matrix-assisted chondrocyte implantation, fibrin fixation, or another contemporary scaffold. Furthermore, direct surgical filling of a visible defect followed by controlled illumination is materially different from injecting a formulation into the general joint space.

In-vitro cellular findings

Bovine chondrocytes encapsulated in the experimental hydrogels remained viable and produced extracellular matrix during culture. DNA, sulfated glycosaminoglycan, Live/Dead, and gene-expression assays provided complementary information about survival and chondrogenic activity [1]. These observations support cytocompatibility of the studied constructs under controlled culture conditions.

They do not demonstrate the behavior of human cells, bone-marrow aspirate concentrate, adipose-derived preparations, platelet-rich plasma, or medications mixed with the scaffold. Each combination can alter osmolarity, pH, cross-linking, cell viability, release kinetics, and regulatory classification. Such uses require direct testing rather than inference.

Can the evidence support office-based use?

At present, no. The published protocol required creation and visualization of a focal defect, precise deposition of a defined precursor, and immediate exposure to 405-nm light. A claim of easy office-based applicability would require evidence that the material reaches and remains at the intended lesion after percutaneous injection, cures uniformly at clinically accessible light doses, does not adhere to unintended structures, and produces benefit beyond placebo or established injectables.

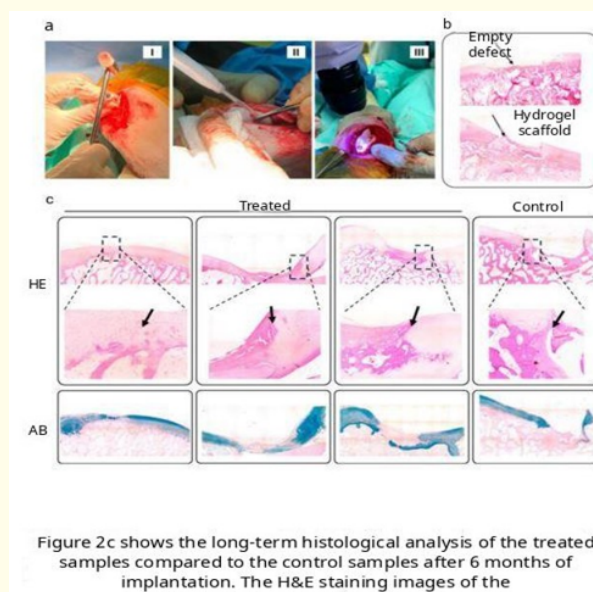
Minimum translational package: Before clinical promotion, the following evidence should be available:

- Full chemical and rheological characterization of the exact marketed formulation, with batch reproducibility and sterile manufacturing data.
- Defined indication, defect morphology, dose, injection route, illumination geometry, energy density, curing time, and post-procedure loading protocol.
- Biodistribution, degradation-product, local toxicity, immunogenicity, genotoxicity, and inadvertent extra-target curing studies.
- Adequately powered animal studies with randomization, blinded validated histological scoring, biomechanical endpoints, and active comparators.
- Regulatory determination of whether the intervention is a device, drug, biologic, or combination product in the intended jurisdiction.
- Prospective human trials assessing symptoms, function, imaging, structural repair, adverse events, and durability.

Scientific and editorial cautions

Terminology should remain consistent. “Hydrogel” is the established material class used in the source study; “viscogel” should be defined chemically if retained. Osteoarthritis, chondromalacia, and focal chondral defects are not interchangeable lesion-size categories. Likewise, a 5-mm experimentally created full-thickness defect is not equivalent to diffuse osteoarthritis.

Claims such as “fewest adverse effects,” “closest to ideal,” “perfect alignment,” “high efficacy,” or “superior treatment” require prespecified comparative data and statistical support. In an exploratory study, calibrated terms such as “suggested,” “was compatible with,” and “warrants further investigation” are more accurate. Product-specific conclusions must be tied to product-specific experiments.



Figure

Conclusion

Photocurable adhesive hydrogels represent a credible strategy for improving retention and lateral integration in focal cartilage repair. The available caprine and *in-vitro* evidence establishes an early proof of concept for the particular MePHa and MePGa systems studied by Karami and colleagues. It does not validate an unnamed or rebranded viscogel, office-based intra-articular administration, combination with orthobiologics or drugs, or clinical efficacy in humans. A defensible translational program should therefore preserve the promise of the platform while clearly separating demonstrated findings from hypotheses and future applications.

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