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In Loving Memory:
Dr. Michael D. Zufelt

Exosome-Based Therapies for Alopecia: A Systematic Review of Clinical Efficacy and Safety

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ABSTRACT

Introduction: Alopecia, including androgenetic alopecia and alopecia areata, significantly impacts quality of life. Current treatments such as minoxidil and finasteride show variable efficacy and may be associated with adverse effects. Exosome-based therapies have emerged as promising cell-free regenerative approaches; however, their clinical efficacy and safety remain incompletely defined.

Methods: We systematically reviewed the clinical efficacy and safety of exosome-based therapies for the treatment of alopecia. This systematic review was conducted in accordance with PRISMA 2020 guidelines and registered in PROSPERO. Searches were performed in PubMed/MEDLINE, Embase, Scopus, the Cochrane Library, and LILACS/SciELO up to September 2025. Randomized controlled trials, non-randomized comparative studies, and observational studies in humans were eligible. Study selection, data extraction, and risk-of-bias assessment were performed independently by two reviewers.

Results: Seven clinical studies involving 323 participants were included, along with one additional pre-clinical study used to provide mechanistic context. The exosome-based interventions evaluated included preparations derived from mesenchymal stem cells, adipose tissue, platelet-rich plasma-associated vesicles, or follicular sources, and were delivered via intradermal injection, microneedling, or topical application. Across controlled and single-arm studies, exosome therapies were associated with improvements in hair density and thickness in several studies; however, the certainty of evidence was low, and results were heterogeneous. Reported adverse events were predominantly mild and transient, including erythema, edema, and injection-site discomfort, with no serious adverse events observed.

Conclusion: Exosome-based therapies demonstrate promising signals of clinical benefit in alopecia, particularly regarding hair density and thickness, and appear to be well tolerated in the short term. Nevertheless, the overall certainty of the evidence is low, limited by small sample sizes, methodological heterogeneity, incomplete outcome reporting, and the absence of long-term safety data. Well-designed, large-scale, randomized controlled trials using standardized exosome characterization and delivery protocols are required to confirm these findings and support safe clinical translation.

Keywords: alopecia, alopecia areata, androgenetic alopecia, exosomes, hair regeneration

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INTRODUCTION

Alopecia, including androgenetic alopecia (AGA) and alopecia areata (AA), is among the most common hair disorders worldwide, affecting both men and women across a wide range of age groups. Beyond its aesthetic implications, alopecia has a substantial psychosocial impact, often leading to reduced self-esteem, anxiety, and impaired quality of life.^{1,2} Current treatment options—such as topical minoxidil/finasteride, oral minoxidil/finasteride, low-level laser therapy, and platelet-rich plasma (PRP) injections—show variable efficacy and may be limited by partial clinical response, adverse effects, or challenges with long-term adherence.³⁻⁵ These limitations underscore the need for innovative therapeutic strategies capable of promoting more consistent and durable hair restoration.

The term “exosome-based therapies” is used in accordance with terminology reported in the clinical literature; however, many interventions represent heterogeneous extracellular vesicle-enriched prepara-



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President's Message

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Spring 2026: Where Integrity Meets Excellence

As spring arrives and I put away my beloved skis after one last run on the slopes, I'd like to take a moment to reflect on our journey together and share our exciting goals for the months ahead.

Excellence Through Education and Innovation

Education remains at the heart of everything we do. As the only hair restoration society accredited by the ACCME, we will continue offering CME webinars. Starting this year, all ISHRS members can attend all CME webinars free of charge, whether or not they participate in the World Congress. This change comes directly from your valuable feedback, and I encourage you to make the most of these learning opportunities to grow your knowledge and skills.

We are also broadening our non-CME webinar offerings. As before, sessions in Spanish will continue to be available, supporting our wonderfully diverse membership. We're also exploring new topics for these webinars to keep things fresh and relevant.

Recognizing the growing influence of AI in healthcare, I am excited to announce the formation of the ISHRS Artificial Intelligence Task Force. If you are interested in AI and hair restoration, please join us—I look forward to your insights as we navigate this important frontier together.

Additionally, to keep us current with the research and provide clear guidance, we have launched a task force to evaluate and provide guidance on the possible adverse effects of finasteride.

Welcoming New Members: Growing Our ISHRS Family

Our Society is the largest international community in our field, and expanding our family remains a priority. In the coming weeks, the Board will review membership applications, thoughtfully considering each candidate and warmly welcoming new members in all categories. Please join me in spreading the word about our great society to prospective members and help us continue building a truly global and diverse network.

Protecting Our Specialty: Fighting the Fight Together

Our "Fight the FIGHT" campaign against black-market clinics and unlicensed surgical delegation is as important as ever. We rely on you to help raise awareness and report any concerns. If you'd like to get involved or contribute to this critical effort, please reach out to our staff—we're stronger when we work together.



... Starting this year, all ISHRS members can attend all CME webinars free of charge, whether or not they participate in the World Congress. This change comes directly from your valuable feedback, and I encourage you to make the most of these learning opportunities to grow your knowledge and skills.

Rio 2026: Where Integrity, Excellence, and Connection Come Together

Save the dates October 14-17, 2026!

Our flagship event, the annual World Congress in Rio de Janeiro, is fast approaching. Under the outstanding leadership of Dr. Maxim Chumak, this year's theme, "Where Integrity Meets Excellence," promises to inspire both professional advancement and camaraderie.

I warmly invite you to take part—whether by presenting your work, networking with peers, participating in pre-courses and workshops, or simply attending. This is a wonderful chance to connect with colleagues from around the world and strengthen our global community.

Looking ahead, the World Congress will continue rotating between continents. Following Rio 2026, we plan to hold the Congress in Asia in 2027, returning to the Americas in 2028. This truly international approach reflects our commitment to inclusivity and access.

Shaping the Future Together

From expanding education and embracing innovation, to hosting world-class events and maintaining the highest professional standards, the Board is dedicated to supporting your growth and the success of our ISHRS. I am honored to lead with integrity, excellence, and a spirit of collaboration.

Let's continue this shared journey throughout 2026. I look especially forward to welcoming you to Rio for our annual World Congress, where we will come together to shape a year of inspiration, connection, and progress. ■

Co-Editors' Messages



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As we put the final touches on this issue, I've had the opportunity to reflect on all that goes into creating not only an educational and informative journal, but also a society that nurtures its members' skills and upholds integrity. One needs to look no further than the President's Message to see this. In it, Conradin von Albertini skilfully highlights a number of ways that the ISHRS is pushing the boundaries—not only to promote the field of hair restoration in an ethical way, but also to support our members through a strong educational foundation. On a personal note, in addition to serving as co-editor for this journal, I also have the honour of serving on a number of committees within the society. It astounds me that, although the calendar year is still relatively young, each committee—a veritable building block of the society—seems to be firing on all cylinders. The time and effort that all the committee members devote to the society is a testament to their integrity and their drive to push the society to even greater heights. I am grateful to the committee chairs for spearheading these efforts with such skill.

As we approach the second quarter of the year, I am impressed to see how the World Congress in Rio de Janeiro is coming to fruition. The planning committee recently met to provide updates on how things are progressing. I was very excited to see the meticulous nature of the planning and learn about the exciting new ideas for delivering what promises to be a fascinating and educational feast. Sam Lam left some big shoes to fill, and I cannot think of a better person than Maxim Chumak to step in and lead the way.

I would also like to congratulate the ABHRS as they stand on the precipice of delivering the first ABHRS exam online. This has required significant effort from the executive committee and will no doubt make the exam more accessible to physicians worldwide, as our society continues to promote the idea that hair transplant surgery should only be performed by educated, ethical surgeons.

Congratulations to Fabianna Acerbi Penha and co-authors for an excellent review on exosomes. Regenerative medicine is the new frontier of this field, and making sure that we have a foundational knowledge on the topic is essential. Another frontier that many of us are trying to master is the skill of not having to shave the donor area when performing hair restoration surgery. In the past, the only option left was FUT surgery, but the advent of long hair FUE has significantly changed the landscape. Georgios Zontos offers his refinements of the non-shaven technique as an option. Conversely, Editor Emeritus Russell Knudsen counsels on the potential perils of pushing those so-called boundaries. Mega and giga sessions are increasingly becoming aspirational goals for both patients and surgeons; however, for many patients, the potential consequences may only become apparent in the years to come.

I extend my sincere thanks to my co-editor for this issue, Brad Wolf. His experience and guidance has been invaluable, and it has been my honour to serve alongside him. ■



Guest Co-Editor: Bradley R. Wolf,
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Thank you to the ISHRS for the opportunity to step back into the role of co-editor for this issue of the *Forum*. It's been a pleasure working with Vikram and the editorial team.

I found Editor Emeritus Russell Knudsen's message to be a thoughtful and cautionary perspective on the growing trend toward giga-session grafting. In March, I attended the 9th Latin American FUE Workshop—beautifully organized by Roberto Trivellini, Ricardo Mejia, and Paul Rose—where the high-volume mega session was discussed. The procedure has evolved to the point that our ability to create density has exceeded the limits of "appropriate" density. I have always believed the theory, "less is more," attributed to the 20th-century modernist architect Ludwig Mies van der Rohe. It takes experience to determine the appropriate density and design based on the patient's age, desires, expectations, density, shaft diameter, hair/skin color contrast, texture, skin thickness, sebaceous activity, and amount of bleeding. The mind is an amazing computer that, with experience, can subconsciously assimilate these variables and make incisions at the appropriate density based on these factors. Less density preserves more donor follicles for future procedures, which will invariably be needed.

As cosmetic surgeons, are we physicians, artists, craftsmen, or architects? Clearly, all of the above, but I consider myself a physician craftsman. Craftsmanship is based on attention to detail and precision, resulting in high-quality results. It reflects skill and artistry, as well as a deep understanding of techniques, materials, and design. It's associated with hand tools, balancing traditional methods with technology to achieve the best results.

Congratulations to Fabianna Acerbi Penha and her co-authors of the excellently written exosome review article. We should welcome any therapy that prevents transplants from being done since a scar is created for every graft removed. Lymphocytes could only dream of causing as much scarring as hair transplant surgeons! As I look back on all my years of moving hair, I am sure hair transplant surgery is the number one cause of scarring alopecia.

Staying on theme, Georgios Zontos's article on non-shaven FUE highlights how thoughtful technical refinements can enhance patient discretion and cosmetic acceptability without compromising graft quality—reinforcing that innovation should serve precision and judgment, not excess.

My heart is warmed reading both Conradin von Albertini's and Maxim Chumak's messages emphasizing integrity. It's the quality I've valued most in all my years of ISHRS service. I am reminded of a quote by Warren Buffet, "Look for three things in a person: intelligence, energy, and integrity. And if they don't have the last one, don't even bother with the first two." May integrity be the guiding light of the ISHRS as we choose our leaders and navigate both the present and the future. ■



Notes from the Editor Emeritus, 1999–2001

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The Problem with Aggression

Having returned from the ISHRS Annual Scientific Congress in Berlin, I found myself troubled by the philosophy of surgical practice that was repeatedly shown, along with the technology that amplifies it.

We saw two exemplary lectures involving giga-session grafting of 10,000-12,000 grafts (over two days) with remarkable results in both the recipient area and the donor area. Impressive results, but is it really the new normal? I believe this trend is troubling from two perspectives: philosophical and practical.

Philosophical Considerations

The aggressive use of single-session grafting is based, in my view, on the heroic assumption that future hair loss is both manageable and acceptable. While this may be the case with our patients over 50 years of age, it is highly unlikely to be the case in younger patients. It requires patient acceptance of lifelong medical management, strict compliance with treatment protocols, and, most importantly, the assumption that treatments will be forever successful in terms of stability.

Giga sessions describe treatment of significant/advanced balding. In younger patients, I describe this as “aggressive balding,” which requires an optimistic assumption about the possibility of long-term stability using current medical treatments. Regenerative therapies are promising, but there is no long-term data that implies improved long-term success. In younger patients with excellent donor density, the temptation is to produce a maximal result in terms of density. Clearly, pre-operative donor density and hair characteristics must be assessed to calculate what is achievable without transferring the balding effect to the donor area by overharvesting. Medium or fine calibre donor hairs are more at risk of “see through” donor depletion.

It is here, in our younger patients, that we face the dilemma of “realistic expectations.” If we treat them as “customers,” then we will be inclined to try and satisfy their sometimes idealistic views of outcomes. Who hasn’t heard a patient say they don’t want lifetime medical treatment, yet still want a single transplant for a lifetime outcome? If we treat them as “patients,” we are obliged to counsel them as to the realities of what lies ahead. Future hair loss is to be expected, and the younger they are, the more likely that outcome. The problem here is that future hair loss does not provide a natural progression of balding. They will bald “unnaturally,” and especially in the crown where lateral and inferior occipital progression of loss provides a balding rim effect as well as deterioration in available future donor supply.

Reduction in donor supply by baldness progression is further amplified by the aging effect upon donor areas. A recent study, presented in Berlin, assessed the donor area of 100 young men between 20-30 years of age. In 60%

of these men, the Telogen/Vellus ratio was less than 4:1! This was irrespective of the degree of balding by Norwood pattern. In other words, up to 25% of donor area hairs were already miniaturising to some degree. Our assumptions about long-term viability of grafts need reassessment. In my view, the aggressive balding patients are generally at higher risk of the phenomenon. The other lesson from this information is that we should counsel our surgical patients that long-term medical treatment of the entire scalp will likely produce a longer-term good result post-operatively.

Another thing that bothered me in Berlin was the demonstration of “AI-assisted” surgical planning tools. Though we might think this of great benefit to our less experienced colleagues as they begin their career, the ones I saw demonstrated were unrealistic. I asked a vendor for the default graft-density setting of the planning software and was informed it was 50 grafts/cm²! He did note that it could be adjusted up or down. This is ridiculously high in my view and dangerous for the less experienced surgeons as it would require very high graft numbers per session to achieve the default outcome.

The dominance of FUE grafting has led some colleagues to state that the expanded donor areas (beard, chest, etc.) allow these giga sessions to be offered. All this does is increase the availability of less than ideal donor hairs that can’t be placed in high visibility areas because of differential hair characteristics compared to scalp hair.

Finally, from a philosophical viewpoint, let’s understand that younger patients are more likely to want higher densities—“as many as you can doc”—and that our older patients are generally more realistic in their expectations. Grafting at 30-35 grafts/cm² usually meets their goals. Not everyone wants to look like Elvis!

Practical Considerations

Giga sessions require long operative times. One of the giga-session lectures described consecutive operative days with a total of 21 hours of operative time! Consider that, for the patient, this is exhausting, they are immobile for great lengths of time (similar to long-haul airplane travel), and it requires significant amounts of cumulative anaesthesia intra-operatively. These are ALL risk factors.

Also consider the effect of surgeon exhaustion on surgical accuracy during harvesting in these giga sessions. Are we really acting in the patient’s best interests?

In summary, it seemed to me, and to other very experienced surgeons near me in the lecture theatre, that the enthusiasm for what is possible has overcome what is sensible for our very balding patients. This is especially so in our younger patients. Our mantra as ethical doctors is “Primum non nocere”—“First, do no harm.” That applies both in the short-term post-operatively as well as the long-term.

The fact that something is possible doesn’t necessarily make it advisable, and should never make it compulsory. ■