Foregen

Regenerative Medicine Solutions for Circumcised Men

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Executive Summary

Foregen is developing a regenerative medicine solution for circumcised men worldwide who seek to reclaim their complete body. We are a 501(c)(3) non-profit organization registered in the United States, with research operations in the European Union. Our leadership, staff, volunteers, and donors come from over 80 countries around the world. This paper outlines the compelling need for foreskin restoration, the ethical foundations guiding our work, and the innovative scientific approach we are implementing to achieve this historic mission.

Our Mission

More than one billion men worldwide are circumcised [1], the majority having undergone the procedure as infants or small children, long before they could consent. Research consistently demonstrates that childhood circumcision can lead to significant physical and psychological consequences [2]. Over time, many of these men come to realize they wish this had not happened, feeling a profound sense of loss for an integral part of their body.

It is precisely to address this deep-seated need that Foregen exists. Our primary goal is to develop a regenerative medicine solution that allows circumcised men to reclaim their foreskin. We are driven by a fundamental moral imperative rooted in principles of justice: to provide a robust solution for those who wish to regain their physical wholeness and to ameliorate the suffering of those who have already been harmed and wronged. We are committed to accomplishing this by developing a comprehensive, tissue engineering solution and bringing it to clinical application.

The Foreskin

The male prepuce, commonly known as the “foreskin,” is a distinct and intricate structure found at the distal end of the human penis. It is highly innervated [3] and serves multiple vital functions, including protecting the glans penis, providing natural lubrication, and contributing to sexual pleasure.

This complex and dynamic structure is comprised of four distinct regions:

1. **The inner foreskin:** This is composed of mucosal tissue [4]. It forms the lining closest to the glans and is characterized by a thick epithelium without skin appendages like hair follicles or glands. It is also highly vascularized. The inner lining is noted to be thicker and firmer, fitting its function.

2. **The outer foreskin:** This is composed of thin, delicate glabrous skin. It is continuous with the shaft skin and is designed to glide freely over the penis. This enables smooth movement and adaptation to changes in penile volume. This layer has very few hair follicles or glands.

3. **The ridged band:** Situated where the inner and outer foreskin meet, this is a distinct, transversely-ridged band of tissue. It marks the transition between the skin and mucosa. When the penis is not aroused, this band is typically located at the very end. It is notably vascularized and contains a high concentration of specialized receptors. It is sometimes also referred to as the frenular band due to its continuity with the frenulum.

4. **The frenulum**: Recognized as a distinct region of the foreskin, the frenulum acts like a "hitch or a check rein" when the glans is bared during erection. It is continuous with the ridged band, and plays a role in the foreskin's overall movement. Many men perceive the frenulum, and the associated "frenular delta," as a highly sensitive area of the penis.

The human foreskin is remarkably rich in specialized nerves and sensory capabilities, making it a critical component for sensation and sexual function. It possesses a highly organized and dense pattern of sensory (afferent) innervation, composed of various specialized encapsulated receptors. These include Meissner's corpuscles, Pacinian corpuscles, Krause-like corpuscles, genital corpuscles, and Ruffini corpuscles.

These specialized nerve endings are vital for transmitting sensations of fine touch, light touch, pressure, and vibration. The inner foreskin, particularly the ridged band and the frenulum, contains a high concentration of these touch receptors, mediating low-threshold and fine-touch sensations [5]. The mechanosensory inputs from these structures are essential for spinal reflexes that regulate movements of intercourse and erection. [6]

In stark contrast, the glans penis has significantly fewer such fine-touch receptors and primarily mediates sensations of deep pressure and pain, with very little fine-touch capability. This difference in innervation between the glans and the foreskin forms a complex sensory platform crucial for normal sexual behavior. The foreskin is recognized as a primary erogenous tissue [7] and its intact sensory architecture is a foundational reference for our regenerative medicine effort aimed at restoring comprehensive sexual sensation.

It is clear that the human foreskin is far more than a simple fold of skin. It is a sophisticated, multi-regional anatomical structure, characterized by its unique composition, gliding function, and, most notably, its highly organized and specialized sensory innervation. This intricate design, critical for nuanced sensation and essential for various aspects of sexual function and pleasure, underscores its role as an integral component of the male anatomy. The permanent removal of such a complex and functional tissue, therefore, represents a significant anatomical and sensory loss, reinforcing the profound need for a restorative solution.

Public Demand

Circumcision involves the surgical removal of the entire foreskin, most frequently performed in the earliest stages of life—within days or weeks of birth. This procedure, at any age, entails immediate consequences such as bleeding, inflammation, and a risk of infection, culminating in the permanent loss of healthy, sensitive, and functionally important tissue [8]. We recognize that the foreskin should not be viewed merely as an appendage, but rather as an integral component of the body's holistic composition. Consequently, its removal constitutes an injury not only to the penis, but by extension, to the body as a whole.

In the U.S., the widespread practice of infant circumcision is primarily shaped by various cultural [9] and political [10] imperatives. Arguments citing health benefits are often employed as a rhetorical justification, rather than serving as elements within a truly unbiased framework for decisions that genuinely prioritize the child's well-being. From our perspective, such rationales do not present a compelling justification to override a child’s fundamental right to bodily autonomy [11].

Beyond infancy, adult men sometimes elect to undergo circumcision when addressing conditions like phimosis or balanitis. However, they are frequently left uninformed about the significant sensory consequences of the procedure, often without a thorough discussion of non-surgical alternatives. Consequently, a substantial number of these men later express deep regret regarding their decision, feeling misled about the full implications. This is understandable, as one survey found that “a higher percentage of circumcised men experience discomfort or pain and unusual sensations as compared with the uncircumcised population.” [12]

We've received numerous personal testimonies detailing adverse experiences from those who wish they had never been circumcised. With their permission, we share some of these accounts:

> *I was circumcised when I was 11. Today it's affecting my entire life. I'm depressed and feel pain that something in my body is missing.*
>
> *I've spent much of my adult life becoming increasingly aware of the physical and psychological impacts it has had on me…Foregen's work in regenerative medicine represents a powerful hope for restoring bodily integrity and improving quality of life for men like myself…Thank you for the groundbreaking work your team is doing.*
>
> *As a person with a Middle Eastern background, it really bothers me that I am missing an integral part of my body…you have no idea how grateful I am that you are helping countless men regain bodily autonomy; I seriously hope that all of this goes smoothly and all goes well as soon as possible.*

The profound impact of this tissue loss is further underscored by scientific findings. A 2007 study, for instance, concluded that circumcision "ablates the most sensitive parts of the penis." [13] This sensory deprivation likely contributes to the widespread desire for restoration.

Confirming this significant demand, a survey we sponsored in 2021 [14] revealed that 16% of circumcised males in the U.S. would prefer to be uncircumcised. Crucially, 38% of that group indicated they would undergo a surgical procedure to regrow their foreskin and fully reverse their circumcision. When extrapolated to the entire population, this represents potentially 7.9 million men [15] who would actively seek the type of regenerative medicine surgery we are developing.

> *I want mine back. It makes me cry every time I think about it—having part of my body forcibly removed against my will as a child, and I can never get it back. It's sick.*
>
> *I would like to be whole again and intact. I'm not happy about my circumcision that my parents consented for me at birth. I'm willing to go anywhere to have this done because I want a fully functional foreskin. I feel that I've lost a lot from losing this part of my body.*
>
> *I got circumcised last year and I deeply regret it. I've been trying everything. I'm currently restoring my foreskin.*

I was circumcised at 29 because I read in many investigations that circumcision helps with STIs and penile cancer, but I have no idea of the different types of circumcisions. I lost almost all my inner foreskin, so my sexual function was damaged. I want to try an experimental procedure to restore the foreskin function. I hope you can help with my situation.

The significant physical and psychological impacts of circumcision, coupled with the widespread distress and regret among affected men, reveal a profound demand for restorative solutions. The personal testimonies underscore the deep desire to reclaim lost anatomy and function, while our survey data quantifies this need, highlighting a substantial population actively seeking a surgical reversal. It is this enduring demand, rooted in the suffering of those who have been harmed, that directly fuels our mission at Foregen. We are committed to developing the world's first regenerative medicine solution to address this critical need, providing a tangible path for men to regain their complete bodily integrity and improve their quality of life.

Our Values

Foregen's mission is grounded in a set of previously established ethical principles that directly inform our work and underscore the urgent need for a restorative solution. These include:

1. The **right to an open future** [16] is an ethical principle asserting that decisions made for a child should preserve, rather than prematurely foreclose, significant life choices and opportunities they would otherwise have as an adult. By circumcising a child, a procedure that is currently irreversible, the individual is deprived of their future option to remain intact. This removes a fundamental choice about their own body. Conversely, if a child is not circumcised, his right to choose is fully preserved; he can always make this decision as a sovereign, self-directed adult. This non-consensual, permanent alteration of a minor's body thus constitutes a pre-emptive harm to autonomy, directly limiting their fundamental right to determine their future bodily state.

2. The **concept of bodily integrity** [17] champions an individual's right to control their own body and remain free from unwanted physical intrusions or permanent alterations [18]. Non-consensual circumcision, performed on individuals incapable of providing assent, irrevocably alters their physical form without their future approval, thereby violating this fundamental right.

3. **Restorative Justice** offers a framework for addressing harm by focusing on repairing the damage done, meeting the needs of those harmed, and reintegrating them into a state of wholeness. Applied to the context of male circumcision, restorative justice acknowledges that a harm was inflicted without consent, leading to lasting physical and psychological consequences. Foregen's work largely embodies this principle by developing a means to physically and functionally restore what was lost, thereby providing a pathway for individuals to reclaim their bodily integrity and a sense of completeness after experiencing an unjust and non-consensual alteration.

When considering these robust ethical principles, particularly the principles of justice inherent in addressing past harms, we believe that providing circumcised men a means by which they may recover as much of their foreskin as possible is not merely a scientific endeavor, but a profound moral imperative.

The Science

Foregen's commitment to addressing the need for foreskin restoration is rooted in the science of regenerative medicine. Our approach harnesses advanced tissue engineering principles to develop a biological solution for those harmed by circumcision. This section details the scientific foundation of our proposed technique, outlining the fundamental processes and protocols that underpin our efforts to bring this innovative solution to reality.

The foundation of our proposed technique is the Extracellular Matrix (ECM). This naturally occurring tissue scaffold, typically derived from human cadavers, is prepared by stripping away all cells containing DNA. This decellularization process renders the ECM acellular, allowing it to be attached to a patient's body without triggering immune system rejection. What remains is a complex biological structure composed primarily of collagen and elastic fibers. To effectively generate and prepare this ECM for eventual surgical implantation, four basic protocols are conducted:

1. **Tissue collection**: the foreskin tissue is taken from an adult organ donor cadaver. The tissue includes all four regions of the foreskin: the inner foreskin, outer foreskin, ridged band, and frenulum.

2. **Decellularization**: this involves removing all cellular and nuclear material from a native tissue or organ while preserving the underlying ECM scaffold [19]. This

scaffold retains the complex three-dimensional architecture, mechanical properties, and bioactive molecules (like growth factors) of the original tissue [20].

3. **Recellularization**: the ECM is re-seeded with the patient's cells. These could come from various sources, including autologous cells or iPSCs (stem cells). The cells are then seeded into the ECM using either a static or dynamic seeding method.

4. **Bioreactor maturation**: after seeding, the cell-seeded scaffold is placed into a bioreactor for maturation. The bioreactor provides a controlled environment that mimics the physiological conditions of the body, which is critical for tissue development. This may include a combination of the following:

    a. **Nutrient and Oxygen Supply**: Continuous flow of culture medium ensures cells receive necessary nutrients and oxygen and that waste products are removed.
    b. **Mechanical Stimulation**: Applying specific mechanical stimuli (e.g., flow/perfusion, stretching, compression) helps the cells proliferate, differentiate, organize, and produce new ECM components, leading to increased tissue density and improved mechanical strength.
    c. **Biochemical Cues**: Growth factors and other signaling molecules can be added to the culture medium to guide cell behavior and tissue development.

    Over time in the bioreactor, the seeded cells interact with the existing decellularized ECM, remodel it, and deposit new ECM components. This process aims to create a fully functional, living tissue construct that can be surgically attached to the body. For tissues like foreskin, this maturation would also focus on ensuring the proper environment for future innervation.

These protocols collectively ensure the creation of a viable, recellularized tissue ready for surgical implantation. This foundational work establishes the biological and mechanical integrity necessary for the successful attachment of the engineered foreskin. Once ready for clinical trials, the surgery will likely involve carefully attaching the engineered tissue to the patient's anatomy, allowing it to integrate with the surrounding structures and establish vital connections with the body's existing systems, including its blood supply. This intricate process is essential for the tissue's long-term survival, successful integration, and proper function within the body.

However, achieving full functional restoration extends beyond successful surgical attachment. A critical subsequent step involves ensuring effective reinnervation, where peripheral nerves from the surrounding host tissue grow into and integrate with the new construct. This complex process is vital for restoring natural sensation and function, and forms a key area of ongoing scientific focus and development within our project [21]. Our current strategy involves facilitating the natural regenerative capacity of peripheral nerves, where an impulse generated in the spine travels down the nerve fibers, guiding new growth into the prepared ECM scaffold [22].

Our Roadmap

This roadmap outlines the critical phases required to translate our innovative regenerative medicine approach from preclinical development through human clinical trials and into widespread clinical application, ultimately making this restorative solution accessible to those who seek it.

1. **Preclinical Research Project**: This initial phase of our roadmap, the preclinical research project, is dedicated to refining and perfecting each of the tissue preparation protocols outlined in the preceding section. It is a critical laboratory-based stage focused on optimizing the methods for decellularization, recellularization, and bioreactor maturation. The purpose of this rigorous work is to ensure the safety, efficacy, and reproducibility of the entire process before any human application. The comprehensive data generated from this preclinical phase will then serve as the foundation for applying for the necessary regulatory approvals to advance to human clinical trials.

2. **Develop Surgical Plan**: This involves developing a comprehensive and precise surgical plan that will guide the implantation procedure in human clinical trials. The plan will detail all necessary specifications for surgeons, including the exact anatomical site and methodology for tissue attachment. A key component will be providing meticulous microsurgical guidance on how to establish a functional vascular network, ensuring the regenerated tissue integrates seamlessly with the patient's existing blood supply. This detailed planning is essential for the safety, reproducibility, and success of the clinical trials.

3. **Contract with Contract Research Organization (CRO)**: Foregen will partner with a specialized CRO to manage the design, execution, and regulatory compliance of our human clinical trials. This collaboration is essential as CROs bring invaluable expertise in navigating complex regulatory landscapes and designing robust study

protocols. They will be instrumental in securing ethics approval, managing the intricate logistics of the trial, and efficiently overseeing the budget and overall operations, ensuring a streamlined and compliant path to clinical application.

4. **Conduct human clinical trials**: This pivotal phase involves initiating and executing the human clinical trials to rigorously test the safety and efficacy of our regenerative medicine solution. This includes recruiting eligible patients, assembling dedicated clinical staff, and meticulously carrying out the surgical implantation and post-operative monitoring according to the finalized surgical and CRO protocols. The data gathered from these trials will be crucial for demonstrating the procedure's success and securing final regulatory approvals for broader clinical application.

5. **Clinical application**: Following successful human clinical trials and the attainment of all necessary regulatory approvals, Foregen's focus will strategically shift towards making this regenerative medicine solution widely accessible. This pivotal phase involves establishing the comprehensive infrastructure and key partnerships required to transition the procedure from research to broad clinical practice, which may include seeking regulatory approval in an international context beyond Europe. As part of this long-term vision, we will also explore and potentially develop advanced solutions like 3D bioprinting to address potential tissue supply challenges, ensuring the scalability and availability of our regenerative solution for all who need it.

Conclusion

Male circumcision performed without medical necessity, particularly when done in infancy or early childhood, has affected the lives of hundreds of millions of men around the world. While often presented as a routine or minor procedure, it can carry lasting physical, emotional, and psychological consequences that are rarely discussed openly. Many men later express feelings of loss, diminished sensation, and frustration at not having had the opportunity to make this decision for themselves. This issue presents a serious and often overlooked medical and ethical concern, one that continues to impact the lives of people who feel they were never given a choice about a permanent change to their bodies.

Foregen is working to directly address this unmet need. As a nonprofit dedicated to advancing the science of regenerative medicine, we are pioneering a biological solution to restore the foreskin in form, function, and sensation. Our research draws on advanced techniques in tissue engineering, with a specific focus on preparing extracellular matrix scaffolds that can be recellularized with the patient’s own cells. This process supports the

development of fully integrated, living tissue that mimics the natural foreskin as closely as possible. One of our core goals is not only to restore anatomical structure, but to support full sensory reinnervation, allowing for a return of natural responsiveness and functional integrity.

This mission is about more than science. At its core, it is the fulfillment of a moral obligation to give circumcised men the chance to reclaim something innate that was taken from them. This profound and often impassioned desire for bodily integrity is understandable, and Foregen's work is founded on the belief that restoration is both possible and an ethical imperative. By building a strong foundation in regenerative medicine technology, collaborating with leading scientists and clinicians, and maintaining transparency with our supporters, we are laying the groundwork for human clinical trials and eventual clinical treatment. With each objective we achieve, we move closer to offering a transformative solution for men around the world who seek healing, wholeness, and bodily restoration.

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