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Novel modalities for hair growth & skin repair

Abstract

Background/Objectives: Evaluate the efficacy and long-term results of established and novel treatment modalities on skin repair and hair growth. Examine the deleterious effects of inflammation in aging and disease. We present a thorough literature review on the reported and actual statistical significance of laser and radiofrequency studies that is often contradictory, on both skin repair and hair growth. Some RF and laser studies postulate short-term improvement on skin repair, and substantial results on hair health, but without following up to control for adverse side effects, effects reversal or reoccurrence or certain skin disorders such as pigmentation which generally reoccur following laser or RF treatments. A main issue pertaining to such technologies is the results of inflammation. Laser and RF companies claim reduction of inflammation. Yet, a large body of research demonstrates significant inflammation increase after trauma-based procedures. A diligent evaluation of other methods and techniques is also conducted based on research and clinical studies presented, with inflammation being the centrepiece.

Methods: In our randomized, double-blind longitudinal clinical research, we followed 22 clinical cases treated with a novel resonance anti-inflammatory technology for up to 4 years.

Results: All subjects evidenced irreversible skin repair and hair growth. Results on hair were slower to appear and ranged from two weeks to one month before observing the full effect. The number of treatments required for substantial repair depended on the chronicity and severity of skin condition, and the extent of hair loss, rather than age. More chronic, difficult cases required more treatments irrespective of whether the subject was younger or older. These results on age-independent skin repair and hair growth advocated for the importance of anti-inflammatory techniques to counterbalance immune insufficiency, age-accumulated oxidative stress, and disrupted cellular communications.

Conclusions: Focus should be shifted from the immediacy of results to the long-term effects of the results with respect to evaluating different treatment modalities on skin repair and hair growth. Inflammation is one of the main reasons for both aging and disease. In assessing the efficacy of a technology, it is important to diligently look for evidence pertinent to the absence of inconspicuous, or insidiously forming inflammation following the procedure, a perspective that most published and unpublished clinical studies fail to consider, since they do not test for inflammatory interleukins or levels of the C-reactive protein that would evidence the presence of inflammation.

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Introduction

Several investigators have demonstrated that "impaired immune surveillance" results in senescent cells, increasing the ageing process.[1,2] Repeated trauma will inevitably increase inflammation undermining immunity.[3–7] There are underreported incidents of laser and RF side effects such as melanoma, hyperpigmentation, hypopigmentation, as well as paradoxical adipose hypertrophy after cryolipolysis.[8–11] Additionally, there is no longitudinal research to support the large corporations' short-term claim that laser and RF rejuvenation and lipolysis treatments reduce inflammation despite the trauma caused. This absent research is necessary because inflammation has been highly correlated with ageing, and is generally considered to be one of the main reasons for ageing, along with increased toxicity and oxidative damage. Several researchers have emphasised the close association of inflammaging with metabolic and other chronic diseases which surface as we get older.[12–16]

Research on the persistence of neuronal communications beyond barriers unveils a vast dynamic complexity of biological communication networks that may behave differently under unforeseeable circumstances.[17–21] This precarious dynamic variability warrants the necessity of longitudinal studies before concluding the efficacy of any technology. Energy devices, stem cells or hormone injection must provide us with 10-15 years of longitudinal research that investigates the long-term results of these procedures before touting their safety and efficacy. Meanwhile, anti-ageing should focus on enhancing cellular repair, health, fitness and wellness without interfering with or traumatising the body.

Hair loss and metabolism

Hair loss can affect self-esteem and self-confidence in both men and women compromising an individual's quality of life. Metabolic dysfunction primarily affects and decreases the anagen-active hair growth phase, while leaving the catagen and telogen phases of cessation of hair growth and follicular rest respectively, unaffected, thus resulting in hair thinning. Hair loss has been associated with metabolic syndrome in both men, pertaining to androgenetic alopecia, and women, who manifest different stages of hair loss as a result of a metabolic disorder. El Sayez et al., compared 45 women with different patterns of hair loss to 45 age-matched healthy women who served as controls. They found a statistically significant correlation between female metabolic syndrome and hair loss.[22] Metabolic and bariatric surgery has been consistently associated with hair loss.[23,24] Hair loss is associated with hypothyroid and hyperthyroid dysfunction. Morinaga et al.,[25] postulated that the same process of hair thinning occurs during both ageing and obesity, due to the depletion of hair follicle stem

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cells.[25] Undermined immunity during ageing and obesity, results in stem cells' inflammatory signals. These findings connect metabolic dysfunction to inflammation which is also considered as one of the principal causes of hair loss.[26]

Inflammation & hair loss

Both male and female hair loss have been associated with inflammatory infiltrates including an increase in lymphocytes and a reduced number of T-cells demonstrating the effect of inflammation on overall immunity.[27] Martinez Jacobo et al.,[28] examined 30 inflammatory and apoptosis genes and documented overexpression of the WNR7A, CASP7, and TNF genes in individuals experiencing hair loss. WNR7A, CASP7, and TNF genes are pertinent to apoptosis and inflammation which interferes with hair growth.[28] Overall hair loss is associated with both psychological and physiological stress, chronic and acute illness, surgical trauma, hepatic and renal failure, systemic lupus, lymphoproliferative disorders and other medical conditions associated with inflammation.[29]

Hair loss treatments: laser and RF

There are several clinical cases touting lasers and radiofrequency treatments for hair growth, even though these technologies have been traditionally used for hair removal. Kinkaid et al, 2023, examined 19 studies to investigate the possible dualistic effect of radiofrequency used for both hair removal and hair growth.[30] Fifteen out of 19 studies described hair removal. A study by Yu et al.,[31] that combined fractional radiofrequency with minoxidil evidenced a mediocre difference between using a combination of fractional radiofrequency with minoxidil vs minoxidil alone. Combined treatment (fractional radiofrequency and minoxidil) increased hair count from 44.12 ± 21.58 to 73.14 ± 25.45. Monotherapy (minoxidil) increased hair count from 46.22 ± 18.77 to 63.21 ± 19.22. These investigators reported statistically significant results as a result of more hair growth in the combined method since they were counting hair. However, based on their data, it is rather unlikely that their combined and monotherapy methods were distinguished by a visible difference.[31]

Laser and RF research, limitations and flaws

There are several issues with both laser and radiofrequency studies in general. The first is that at least 90% of these studies are based on research financed by laser or RF large corporations who also pay a fee to the journals for the study to be published. So there is no thorough independent peer review because the scientists' peers are also looking for a chance to be hired by large corporations and get paid to do research. In other words, there are conflicts of interest in both the scientists who conduct the research and those who review their papers. Which scientists will give an honest opinion that conflicts with the interests of a large corporation at the expense of never getting another chance to do research for this or any other laser or RF Company? The brave and honest will be blacklisted and eventually lose their voices. Irrespective of how prestigious the scientists who compose this funded research are, funded research is advertising.

The second issue pertains to the statistical significance reported in financed laser and RF studies. Results appear to be exaggerated when one examines the research data. For example, Koike's at al team, 2012, 2014, who looked at the effects of the ND Yag laser on keloids and hypertrophic scars, report a statistical significance of $p>0.01$. This signifies that over 99% of their cases got a reduction of their lesions. However, a thorough examination of their data shows that only 8 out of 22 subjects had a clear reduction of their lesions – this is only 36%. Ten of these subjects had a slight reduction, which is 45%, and 4 of these subjects showed no change (18%). In conclusion, only 82% of the subjects had some change in their lesions. Even if one adds both the clear and the slight reduction of these subjects' lesions, the results cannot amount to over 99% and the results reported are invalid.[32] Overall, laser and RF studies report modest results, where 34-24% of the subjects show no change after the treatment and keloids reoccur in 21-34% of the subjects' treated.[33–35]

The third issue is the lack of long-term studies to validate the assumed efficacy and safety of energy devices. There are several reports of escalated inflammation following radiofrequency procedures, so using radiofrequency for hair growth which is compromised by inflammation, is an oxymoron.[36–39]

Hair growth, skin repair and stem cells

Stem cells offer tantalizing prospects for anti-ageing and regenerative medicine. They are used for skin repair, hair growth and the maintenance of various adult tissues and organs. They can modulate numerous incurable diseases such as heart conditions, diabetes, and brain injuries etc.[40,41]

The coin has two sides, and stem cells focus only on the positive one– the miracles of transplanting undifferentiated embryonic stem cells to cure a variety of diseases, without bona fide evidence from large well-controlled studies with proven validity and reliability. Even mesenchymal stem cells (MSCs) which are relatively safe from malignant transformations, and do not stir up ethical controversies, have limited clinical usefulness due to cellular senescence that impairs their differentiation potential leading to uncontrolled proliferation and tumour formation. Ageing is not the only process that diminishes the function of MSCs. Their phenotype is affected by the donors' heterogeneity, the culture condition, and the cell passage in the body.[42–44]

The key factor that determines the usefulness of stem cells is differentiation. Cells must differentiate to become specialized cells, such as skin, bone, muscle, blood, immune cells, etc. Arrested differentiation leads to uncontrolled proliferations which results in the formation of possble malignancies.

Cellular differentiation depends on the increased ratio between:

I. Mitochondrial differential that promotes activity, and

II. Nuclear differentiation that prevents activity.

Embryonic stem cells have a low ratio and therefore a compromised differentiation potential, due to low mitochondrial content. Mutations in nuclear genes coding for mitochondrial proteins decrease the differentiation rate leading to neoplastic growth, another word for tumours that may be benign, or malignant cancers.[45–47]

Embryonic stem cells (ESC) are established by using cells obtained from the inner cell mass of an early-stage human or animal embryo. Many protocols have been established for the differentiation of human or animal ESCs into numerous mature and functional cell types. Nevertheless, clinical application of ESCs, especially in the anti-ageing industry remains controversial due to concerns about teratoma formation and ethical issues raised from the embryonic source of the tissues.[48–52] There is normal and uncontrollable proliferation that aimlessly continues with deleterious effects on the body. Proliferation and differentiation are like a seesaw: when one goes up the other goes down.[53] Cellular proliferation increases with

age while differentiation decreases which is why cancers are more prominent in older individuals. Importantly, differentiation is blocked in cancer cells which have an unlimited proliferative capacity to form teratomas. Cellular proliferation without differentiation is dangerous. We don't need more cells. We need more **differentiated** cells.

One of the main difficulties with Embryonic Stem Cells is immunorejection. Promoting stem cells' graft acceptance is more difficult than host acceptance of a vascularized organ like a heart. Some researchers have used antibodies to block normal T-cell activation to reduce immunorejection and increase the EMC's systemic acceptance. However, such techniques win the battle over immunorejection and, by incapacitating the immune system, they lose the war over tumours growing unobstructed since the immune soldiers are temporarily paralyzed. Tumorigenesis is the main danger with EMC's and a worse problem than immunorejection.[54] Anti-ageing professionals should know that; yet, they focus on immunorejection in the pursuit of fast instant results at the risk of exposing their patients to eventual cancers. This fast instant results' wish-fulfilment is the crux of social brainwashing that places beauty above health, and temporary symptom improvement over overall wellness.

Gurdon and Yamanaka received the Nobel Prize in Physiology or Medicine 2012 for their discovery of reprogramming mature cells to become "induced Pluripotent Stem Cells (iPSCs).[55] Takahashi and Yamanaka reprogrammed terminally differentiated fibroblasts by the transduction of four defined transcription factors Oct ¾, Sox2, KLF-4, in addition to LIN-28 and Nanog, successfully producing iPSCs' differentiation into neurons, cardiomyocytes, retinal epithelial and pancreatic islet.[56] iPSCs win the war over ethical issues attached to EMCs but being pluripotent, they also have the disadvantage of teratoma formation. Bottom line, stem cells are useful and miraculous until they are not.

Resonance skin repair and hair growth

In the current study, we used a new ultra-low energy nanotechnology device originally invented for research purposes in London University and was upgraded over a period of 28 years. It is primarily based on three basic theoretical principles.

Principle 1. Electron-gated ion channels at energies below thermal noise

While strong oscillating electromagnetic fields have shown no easily measurable or obvious effects on humans or living systems, much weaker oscillating fields have been shown to affect living systems in often dramatic ways.[57] In his book "Electron Gated Ion Channels" Wilson Ranston, (2005) presents a new quantum-mechanical approach to the intrinsic simplicity of electrons controlling sodium, potassium and calcium ion channels at ultra-low energies below thermal noise, elucidating mechanisms important to cellular function and signalling. At those energies, below thermal noise, the ion channels of the cells open up, the way you can remotely open up your garage door. Ion channels are like the doors and windows of the cells. When they are wide open, signals that will resonate and repair signalling pathways can be readily absorbed.[58] Signals that are incompatible with the system will not resonate and will be discarded as noise or waste. So the research on signal synthesis must focus on the compatibility of these signals with the biological network. Only blueprints of biological signals will resonate. There is an unlimited number of wrong combinations that will make no difference and only one correct solution. The body will only accept signals that are in sync with the biological network.

Principle 2. Time reversal is only possible in molecular mechanisms

The possibility of time reversal increases with simplicity and decreases with complexity. Simple molecular mechanisms like free radicals can go back in time and reinstate themselves as stable molecules as a result of anti-oxidant electron donation. This time reversal process can be observed with AMP being transformed forward into ADP and ATP, and backwards into ADP and AMP with the simple addition or subtraction of a phosphate. Similar time reversal processes can be observed with G proteins and several other microscopic biological mechanisms. Time reversal becomes impossible with increasing complexity because as cells combine to form organs or whole entities they turn into Gestalts which are more than the sum of their parts and persist despite changes that may occur within their framework. This molecular time-reversal process has been recently explored by several Nobel Prize-winning studies.[59–64]

Principle 3. Cellular communications reflect intertwined dynamic networks with predictable and unpredictable aspects

The Nobel Prize in Physiology or Medicine 2013[65] describes transport and delivery of cellular signals resembling a public transport system. Defective signal transport occurs in a variety of diseases including a number of neurological and immunological disorders, as well as in diabetes.[66–69]

Several years ago, we thought that within the nervous system, neurons could only transmit information via electrical signals limited to their physical connectivity, acting like analogue telephone landlines. Since then, new research has revealed that glial cells transmit signals without any physical connectivity acting like cell phones that can transmit signals through long distances. The concept of pure neuronal networks is now expanded to include neuron-to-neuron, neuron-to-glia, and glia-to-glia networks that significantly increase the complexity of signalling connectivity. The type of glial cells restricted to the brain and spinal cord are called astrocytes. So in addition to the "electrical excitability of neurons, there is a calcium-based cellular excitability or astrocytes which add the process of "gliotransmission" to that of "neurotransmission."[70,71] Chaban et al (2013)[72], demonstrated that cells can also engage in cell-to-cell signalling in the absence of any physical contact between them, demonstrating physically disconnected, non-diffusible cell-to-cell communications.[73]

The cellular signalling communication network can be seen as a microcosmos reflecting traffic events that are divided into predetermined predictable events such as traffic lights and non-predictable events that emanate from the variety of car types, car conditions, speed, drivers and driving styles. Research to date has mostly provided knowledge for predictable events with an increasingly sophisticated yet limited, dynamic volatility confined by the traditionally recognized signalling pathways. Chaban's et al., findings[72] on the persistence of neuronal communications beyond barriers unveil a vast dynamic uncertainty of the biological communications network that may behave differently depending on the situation. This precarious dynamic variability warrants thorough scrutiny and methodical observation before concluding the long term efficacy of any technology presented in the treatment of wounds or any other disorder.

Results

A total of 22 subjects 12 females and 10 males participated in this longitudinal study, aged 45-79 years old. The subjects represented

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cases offered by 6 different clinics. None of the subjects was aware that they would be included in this study when they signed the consent forms to receive their treatments. None of the doctors or clinicians who performed the treatments knew that their patients would be included in a research study when they performed the treatments or when they took the photos. Therefore, this was a double-blind study.

Twelve of these subjects received 10 skin rejuvenation treatments per year for a period of 4 years. Before and after photos for skin repair were taken 4 years apart (Image A, image B).

Image A (left): Before photo was taken on 12-22-2017. The after photo was taken on 10-29-2022.

Image B (left): Before photo was taken on 3-4-2018. The after photo was taken on 10-29-2022.

Eight of these subjects received 5 treatments for hair growth. After photos of hair growth were taken 4 months later. Subjects received five treatments. Hair seemed to instantly respond to the resonant signals of the treatment. Hair growth was substantial even after the first treatment. The hair grew faster and it was visibly thicker (Image C, Image D, Image E).

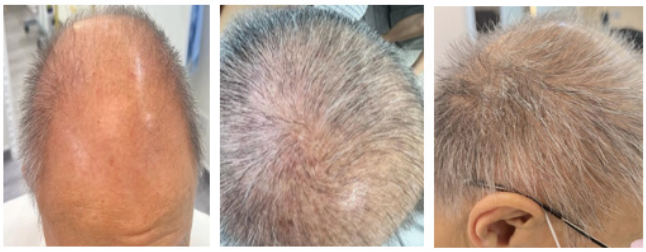

Image C (Below): 5 treatments of hair growth within 4 months.

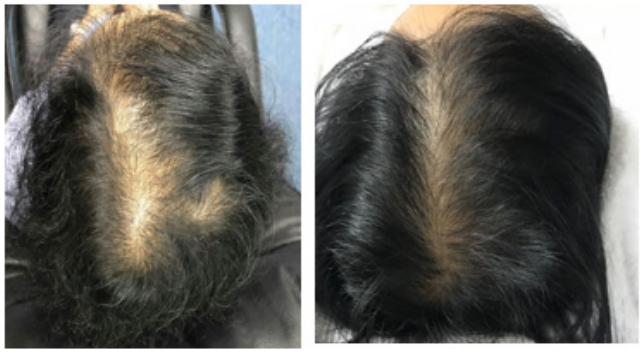

Image D (Left): 5 treatments within 4 months.

Image E (Left): 5 treatments within 4 months

Two subjects treated for Keloids, showed significant improvement after six treatments with no reoccurrence of the keloid scar for a period of three years following the treatments (Image F).

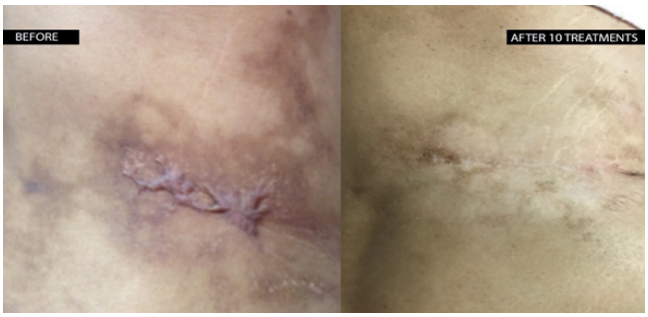

Image F above. Keloid scar treatment after 10 treatments. No reoccurrence of the keloid scar for at least three years.

Discussion

There are novel rejuvenation and hair growth technologies that are underreported due to insufficient funds for large expensive studies, or because the technology inventors are reluctant to invest in marketing because they capitalize on financing more research. All these health and immunity-enhancing technologies are shadowed by the glamorous spotlights of widely publicized research financed by large laser and RF corporations who are determined to prove the counterintuitive concept that trauma delays ageing. They feature 20-year-old models who had never had the procedure, and proudly present before and after pictures with hardly noticeable results, reminiscent of how easily the public is fooled by the Emperor's (non-existent) "new" clothes.

In evaluating the positive effect of energy devices, one must consider the fact that the presence of inflammation after a traumatic procedure gives a false sense of rejuvenation as the prolonged swelling masks fine lines and wrinkles. Rajan et al.,[74] have postulated that contrary to the general belief that inflammation is a necessary phase of skin repair, in fact, the immune cells that regulate the inflammatory phase to remove invading pathogens are not necessary for skin repair. Instead, inflammation may be responsible for scar formation and may often prevent wound closure.[74] Importantly, there is substantial evidence that the main cause of aging and hair loss is inflammation.[12–14]

There are some articles claiming that laser and RF treatments are generally safe with sporadic serious side effects like cancer, melanoma or other skin diseases. However, there are no articles confirming that the rejuvenation effect noticed shortly after laser and RF treatments endures. Overall, there are no studies that demonstrate the long-term efficiency of energy devices on skin and hair. Importantly, there is no documentation of a sustained anti-aging effect five, ten, or fifteen years after laser and RF treatments or whether such treatments speed up the aging process, instead. Unless laser and RF corporations provide us with long-term studies that trauma-based procedures actually delay ageing, we must consider the obvious alternative: A healthy person looks younger than a sick or traumatised one. Health and strong immunity delay ageing. Anything that compromises immunity, such as trauma, will eventually have deleterious effects on the skin and hair.

Our current research included a small sample, courtesy of several clinics that participated in this study. The sample on the keloids was too small to calculate significance. Both hair growth and facial rejuvenation were visibly pronounced, and evidenced substantial improvement with time. More longitudinal research on this or similar health-promoting anti-inflammatory technologies is necessary to expand knowledge and offer external and internal validity to our currently reported results.

Conclusion

Focus should be shifted from the immediacy of results to the long-term effects of the results with respect to evaluating different treatment modalities on skin repair and hair growth. Inflammation is one of the main reasons for both aging and disease. In assessing the efficacy of a technology, it is important to diligently look for evidence pertinent to the absence of inconspicuous, or insidiously forming inflammation following the procedure, a perspective that most published and unpublished clinical studies fail to consider, since they do not test for inflammatory interleukins or levels of the C-reactive protein that would evidence the presence of inflammation.

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Statement of ethical approval

This study was performed in accordance with the ethical standards of medical research involving human participants as cited by:

Ethical principles for medical research involving human subjects

American Psychological Association (APA)

ELLIOS Research Department for Development and Invention of Innovative Technology.

Conflict of interest

The author declares no conflict of interest. This study was conducted by independent operators who were not employed or contracted by the author.

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