

## New idea for hair transplantation to preserve more donor hair follicles

### ABSTRACT

Higher risk of rapid progression in alopecia or male pattern baldness was observed in men who had family history. This could result from accumulation of DHT in hair follicles. Hair follicles on frontal region are more vulnerable to DHT. With development of minimal invasive hair transplantation surgery, hair follicles transplantation could be performed from frontal or occipital region to frontal region. However, limited hair follicles remained a problem. With development of technology of vitrification, we suggested extracting hair follicles from frontal region without affecting the appearance and preserving them with vitrification when the patient was young. When alopecia progressively developed, these extracted hair follicles would increase the donor number of hair follicles used for transplantation, which could extend longer dense hair appearance.

### Introduction/background

Genetic inheritance can lead to androgenetic alopecia or male pattern baldness. Considerable amounts of research in this area have discovered that there is an increased activity of hair follicle matrix 5 $\alpha$ -reductase and 17- $\beta$  Hydroxysteroid dehydrogenase in the bald area [1–4]. However, no conclusion is made as no one is certain whether the results are the root or the outcome of the incidence of disorder. Nevertheless, one thing is certain – hair follicle atrophy is caused by male hormones, particularly dihydrotestosterone (DHT) [5–8] Fig. 1.

There are 5 $\alpha$ -reductase in the hair follicle cytoplasm, which converts testosterone into dihydrotestosterone (DHT). DHT enters into the cell nucleus of hair follicle causing a strong inhibitory effect on the metabolic system that prevents protein synthesis in the hair follicle and stops hair growth, which is followed by the gradual disappearance of atrophy [9].

Baldness among male subjects commonly starts from the forehead to the head and temporal bones. This is due to the fact that the resistance to DHT of hair follicles in these areas are quite weak. Male subjects after adolescence produces a lot of male hormones which are converted by 5- $\alpha$  reductase DHT, producing a strong destructive force towards the hair follicles. Once the hair follicles begin to accumulate a large amount of metabolite DHT, the hair follicles shrink and deteriorates, thus, resulting in the start of hair loss. The hereditary male pattern baldness begins to manifest after puberty. The older a person gets, the greater the DHT accumulation is, and the more apparent is baldness [10,11]. Hair growth in different scalp regions have varying immunity to male hormones [12]. The occipital region has higher resistance to DHT and is less affected by male baldness. In minimally invasive hair transplantation surgery, hair follicles are, therefore, extracted from the occipital region and implanted in the hair loss site achieving a long-term hair growth effect. However, the original hair on the frontal scalp region does not have the characteristics of the long-lived hair follicle in the occipital region. If proper care is not exercised, there is still the possibility of hair loss. To prevent the original hair from falling out, regular diet and rest must be strictly observed and doctor's instructions must be rigorously followed. Generally, the number of hair transplants recommended by doctors depends on the age of the patient and the

amount of hair needed. If the patient is young, it is expected that there will be inevitable changes in hair loss in the future. Therefore, considering the unpredictable future, physicians will suggest two or more transplantation, in which case, the hair follicles are sometimes not enough [13–17].

### The hypothesis/theory

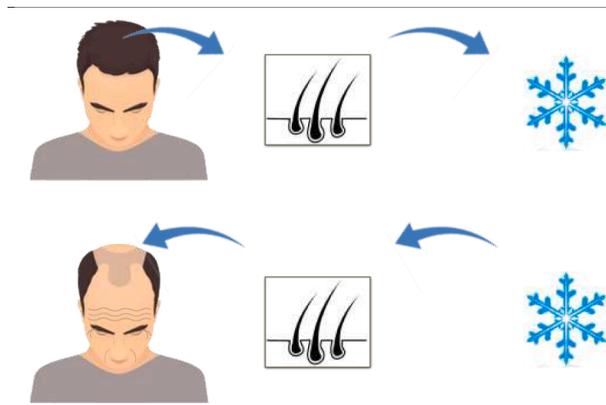
Considering men with family history of androgenetic alopecia, who are future patients with a high chance of rapid progress, it is suggested that dense hairs from the frontal hair follicles be extracted, then frozen, in adulthood using FUE without affecting the appearance. When male alopecia occurs, perhaps ten years later, these patients will have an increased number of seedlings for hair transplant and decrease the possibility of insufficient number of hair follicles, thus, extending the dense hair appearance for longer years.

Upon reaching adulthood, part of the frontal hair follicles is extracted without affecting the overall appearance. The hair follicles are then frozen in stock. If the progression of the disease is fast, the hair follicles in stock can be implanted. Due to the rapid development of the disease, another transplantation might be required. The drawback of multiple operations is the insufficient amount of hair follicles. With this procedure, the number hair transplantation can be increased and delay the disturbing occurrence of androgenetic alopecia.

Certainly, it is necessary to be aware that both the frontal and occipital hair follicles have different characteristics – frontal hair follicles have higher probability to fall off whereas occipital hair follicles are not likely to fall off.

Storing hair follicles to be used 10 years later, at the age to care about appearance, will give the subject the opportunity to look better with the advanced cryopreservation technology and hair-planting technology. It is possible to gain a few 10 or 20 years of better appearance, which is good news for the patients.

It should be noted that the frontal hair and the occipital hair should not be implanted interchangeably because their different characteristics. It is suggested that occipital hair follicles be implanted according to the existing consensus and aesthetic requirements while the frontal hair follicles are homogeneous and does not increase in density.



**Fig. 1.** Extracting hair follicles without affecting appearance when young in patient who had strong family history of alopecia, and preserving them with vitrification technique. It will be more hair follicles available for transplant in the future.

### Evaluation of the hypothesis/idea

The hypothesis comes from the advancement of the freezing technology of the organization, such as the egg freezing also known as mature oocyte cryopreservation [18–20]. Due to the large volume of eggs and embryos, they easily crystallize during the freezing process thus damaging the specimen. It was not until 1986 that a successful pregnancy was reported using thawed eggs [21]. Compared with sperm cells, cryopreservation of eggs is more difficult and less efficient. In the recent years, vitrification freezing technique is developing rapidly. The cell dehydration and ultra-fast cooling technology effectively reduced the formation of ice crystals in the freezing process, thus significantly improving the survival rate of eggs and embryos being thawed. The first successful record of this technique in freezing human eggs with live birth were recorded in 1999 [22]. Research also proved that live birth from eggs frozen through vitrification technique does not differ from fresh eggs. Therefore, in 2012, the American Society for Reproductive Medicine recognized the use of vitrification technology for clinical work [23]. The cryopreservation of spermatozoa and embryos is routinely performed by the center and the vitrification freezing kit used is the most efficient commercial kit on the market [24]. Vitrification egg freezing is used in egg donor banks, extension of child-bearing years, storing extra embryos during IVF treatment, and preserving fertility before cancer treatment.

Embryo freezing applies to those: with residual embryos, with excessive ovarian stimulation, who are not conducive to embryo transfer or implantation, who have temporarily suspended treatment due to illness, and who become infertile due to autoimmunity. Sperm cryopreservation targets include: sperm donors, planned delay in child-bearing, treatment for illnesses such as cancer, and IVF treatment sperm storage.

This mature method can be applied to the preservation of hair follicles. Upon reaching adulthood, part of the frontal hair is extracted without affecting the overall appearance. Then the extracted hair follicles are frozen and stored in bank. In case of rapid development of the disease and the occipital hair follicles are not enough for transplantation, the extracted and stored can be used to provide part of the volume and extend the life expectancy of the hair growth.

### Empirical data

Survival rate is very important target for baldness. Under normal conditions, the survival rate of implanted hair follicles should be more than 90% or even close to 100%. But with the frozen hair follicles, it is uncertain. In an article on this study published in 2008, cryotop frozen donated eggs were used to assess egg survival rate, fertilization rate, division rate and embryo development rate by thawing vitrified frozen

eggs. The obtained data were then compared with the data of fresh eggs for differences. This study allowed us to have a better understanding of whether cryotop vitrified freezing technique can be properly applied to the preservation of germ cells [25]. In this literature, the women who donated eggs and who received eggs were used as the subjects. The result shows that out of 231 matured vitrified frozen eggs, 224 eggs survived after thawing resulting in a survival rate of 96.6%. After microinjection fertilization, 171 eggs were fertilized leading to a fertilization rate of 76.3%. The fertilization rate, however, of fresh eggs in the control group was 82.2% and there was no significant difference between the two. Both the fertilization abnormal rate and DG rate are similar.

Vitrification technology has a high concentration of cryoprotectant which is toxic to the cells. When the rate of cooling is not achieved, it causes an irreversible freezing damage. At present, a combination of various cryoprotectants are being utilized to disperse the respective toxicity and to maintain the concentration during vitrification freezing. Through the improvement of the freezing device, these two possible injuries are greatly evaded. The vitrification process uses Cryotop transparent film-like carrier, with a relatively small volume, to quickly achieve the desired temperature bypassing the temperature where crystals are formed (between 15 °C and –5 °C). In addition, the thawing temperature was also effectively improved to prevent the possible formation of ice crystals during thawing. Another advantage is reducing the permeability of the cryoprotectant by less than 30%, thereby lessening its toxicity to cells. Therefore, in this study, the freezing and thawing rate are effectively improved and the cryoprotectant concentration are lowered to decrease the damage caused to the eggs during the freezing and thawing process.

The attained survival rate, fertilization rate, embryo division rate, blastocyst formation rate and other subsequent developmental abilities of thawed eggs in this literature have been quite promising, thus, people are beginning to be optimistic about this technology. We, therefore, believe that the survival rate for hair follicle implantation would also be reasonable.

### Consequences of the hypothesis and discussion

The current development on androgenetic alopecia research is based on enzymes, genes, and stem cells [26]. We are aware that baldness implant surgery is basically a work of redistributing of autologous hair. Therefore, difficulty arises for those with serious hair loss problem because the occipital hair follicles are limited. In view of this situation, the current study of baldness is oriented towards [1] the cultivation and transplantation of stem cells or dermal papilla cells [2]. The replication and regeneration of hair follicles are developed in several directions. It is hoped that in the future, only a small amount of hair follicles will be

used. Through cell engineering, it will be possible to raise large amount of dermal papilla cells and use those produced cells for transplantation in the bald area. However, before this breakthrough, it is possible that our hypothetical approach may be of some help.

#### Declaration of Competing Interest

None.

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