Application of Rapid Prototyping Technology in Development of Continuous Implanters for Dermal Papilla Cells

Yih-Lin Cheng and Yao-Chung Liang

Department of Mechanical Engineering, National Taiwan University of Science and Technology

ylcheng@mail.ntust.edu.tw

Abstract - The existing popular ways to treat androgenetic alopecia have their limited effects. The recent study found that implanting massively in-vitro proliferated dermal papilla cells into the bald areas could induce the transdifferentiation of epidermis in to hair follicles. However, there are no suitable continuous implanters for implanting the dermal papilla cells aggregates to achieve shorter preparation time, higher implant speed, and controllable implanted depth. In this research, continuous implanters which have cell storage capability were developed to place semi-solid dermal papilla cells in a cartridge and push the cells into the derma through a needle. Three designs were investigated—auto-expand type, bar-cartridge type, and rotary-cartridge type. With the help of Rapid Prototyping technology, the prototypes of implanter were able to generate for simulated implantation tests. Implanting efficiency and implanted depth were two major concerns in the evaluation. The results showed that bar-cartridge type implanter is the most feasible and suitable design among three for continuously implanting the cell aggregates.

Keywords – Rapid Prototyping, Implanter, Alopecia, Dermal Papilla Cells.

I. INTRODUCTION

Androgenetic alopecia happens quite often to men all over the world. Finasteride, minoxidil, and hair transplantation are the popular ways to treat it, but each has its limited effects The recent study [1] found that implanting massive in-vitro proliferated dermal papilla (DP) cells into the bald areas could induce the transdifferentiation of epidermis into hair follicles. The approach to implant the DP cell aggregates is either by surgery or by syringe, which is time consuming in preparing and in loading the cells. The existing hair transplant tools, such as Choi hair transplanter [2], hair transplanter pen [3], and KUN implanter [4], are designed for follicles and usually are discrete transplantation at a time. A hair implanter carousel [5] was proposed in 1998 for continuous hair transplant, but no commercial products are available afterward due to the fabrication difficulties. In other side, other implant tools, such as gene gun [6], solid-drug implanter [7], and RALGRO [8], are not suitable for DP cells implant, either. Therefore, there is a need to develop a continuous implanter for DP cells aggregates to shorten the preparation time, to accelerate the implant speed, and to well control the implanted depth. In this research, three types of continuous implanters were designed for DP cells. Rapid prototyping technology was utilized to fabricate components of implanter prototypes, and the preliminary tests were conducted through these prototypes to compare the three designs.

II. IMPLANTER DESIGN

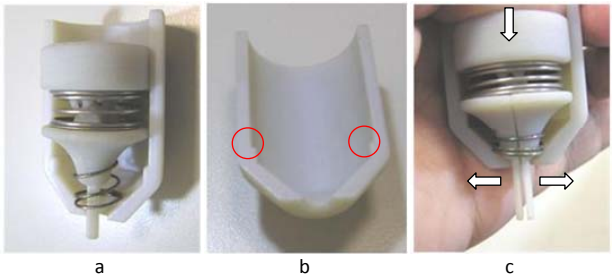
The concept of continuous implanter design is to place semi-solid DP cells or cultivate them directly in a cartridge, and an auto feed mechanism is utilized to push the cells aggregates into the derma through a needle. The implanted depth was set to be 2 mm, which is in the dermis. Since the tissues in dermis are dense connective tissue, traditional syringe which uses air or liquid behind the piston to push out the DP cells is very likely to clog the needle. Therefore, a stiff acupuncture needle was adopted as a push-out needle to replace gas or liquid to push the DP cells out through the needle pierced into skin. The clearance between the push-out needle and pierced needle can help the air out and make it easier to send the cell aggregates into the dermis. For comparisons, two needles combinations were adopted as shown in Table 1.

Table 1 The sizes of two needles combinations

	Thick needles	Fine needles
Push-out needle diameter	0.5 mm	0.3 mm
Pierced needle diameter	0.584 mm	0.318 mm

A. Design 1— Auto-expand Type

The first design considers to mix DP cells aggregates in gel and load into the tube in the implanter. The implanter will need to pierce the derma, expand the pierced hole, push the DP cells gel in, cut off the gel, and return to initial position for next implant cycle. Two major mechanisms were required to perform the actions—auto-expand mechanism (Fig. 1) and pushing mechanism. When there is a pressure from the top, the auto-expand mechanism will expand the two-half needle holders. After the pressure disappears, the spring will push the internal structure back to the initial status and implanter is ready for the next round implantation. The CAD and exploded view of the auto-expand type implanter is shown in Fig. 2 and 3.



a b c

Fig. 1 Auto-expand mechanism

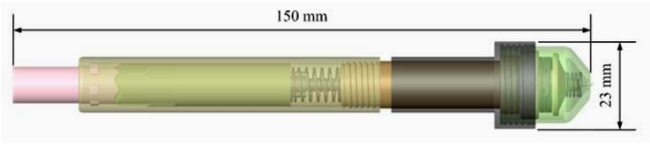


Fig. 2 CAD file of the auto-expand type implanter

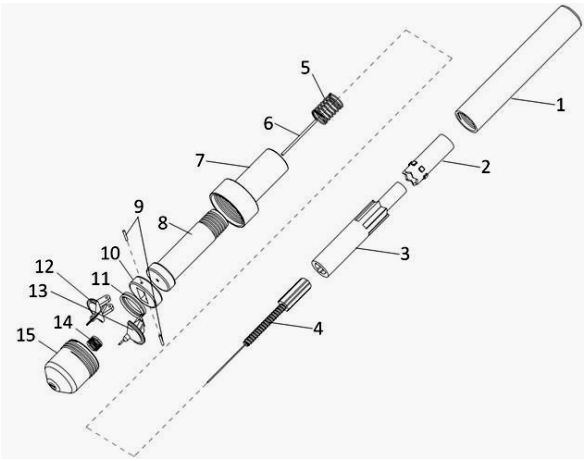


Fig. 3 Exploded view of the auto-expand type implanter

B. *Design 2— Bar-cartridge Type*

The second design considers to place DP cells in a bar cartridge. A thin layer of biomaterial can be coated on the bottom of the cartridge, so that the DP cells can be either place in it after culture or cultured in it directly. Each unit in the cartridge is cone-shape (Fig. 4) to help holding the aggregates. The design of bar-cartridge type implanter is shown in Fig. 5 and 6. When external force is applied to the implanter top, the bar-cartridge pushing mechanism will clockwise rotate certain angle and push out the DP cells. After the force is released, the mechanism rotates counter-clockwise back and moves the cartridge to next unit.

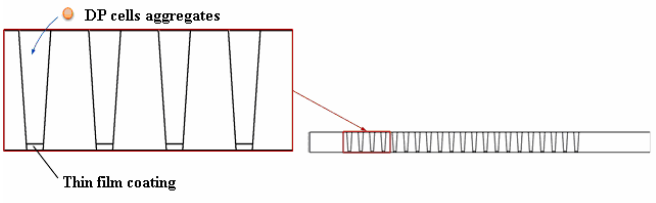


Fig. 4 The design concept of the bar-cartridge.

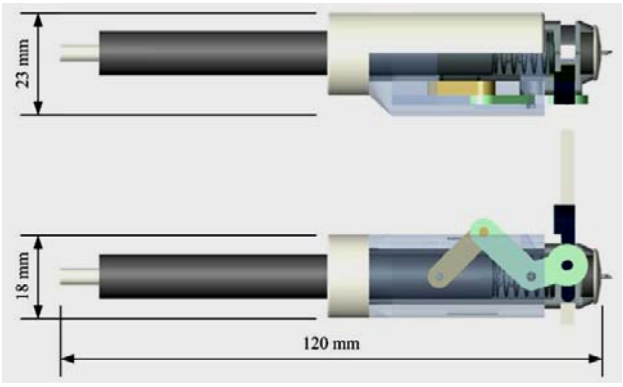


Fig. 5 CAD file of the bar-cartridge type implanter

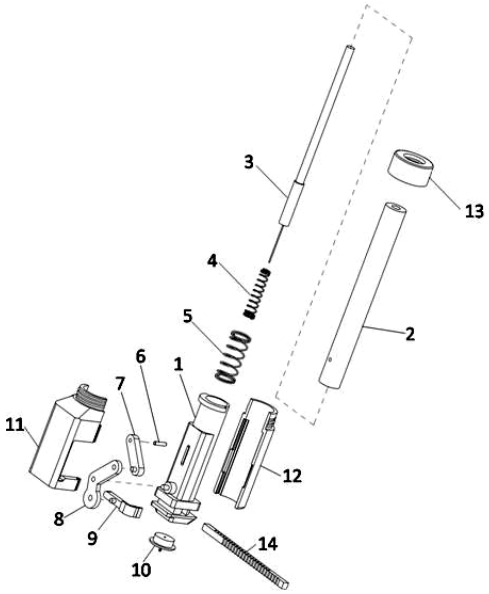


Fig. 6 Exploded view of the bar-cartridge type implanter

C. *Design 3— Rotary-cartridge Type*

The third design replaced the bar-cartridge to a rotary-cartridge (Fig. 7), for considering holding convenience and reducing vision block during operation. The design is shown in Fig. 8.

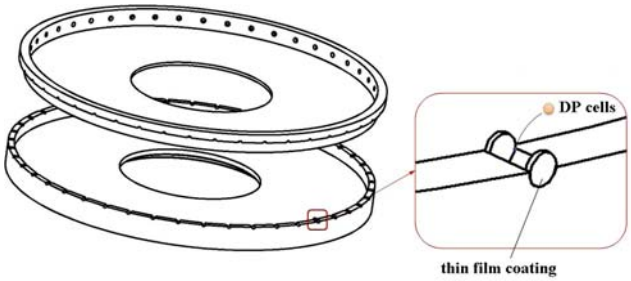


Fig. 7 The design concept of the rotary-cartridge

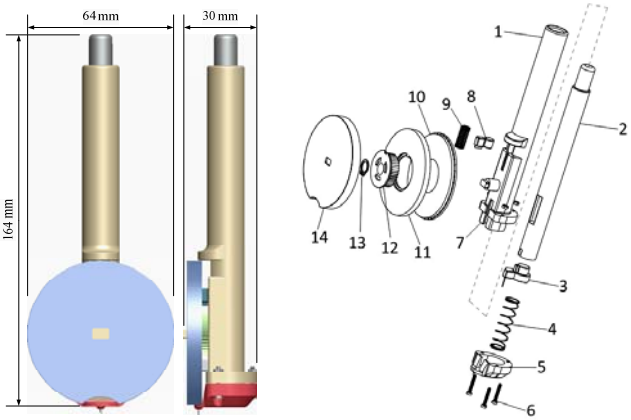


Fig. 8 Design of rotary-cartridge type implanter

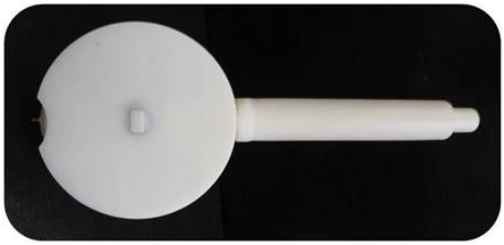
III. IMPLANTER PROTOTYPES

Rapid Prototyping (RP) technology was used to fabricate the components of three implanters to generate prototypes for testing and comparison. A commercial RP

system, Objet's EDEN 330 (Objet Geometries, Inc., Israel), was utilized. Objet's PolyJet™ process jets photopolymer in ultra-thin layers, 16 μm, layer by layer. Each layer after jetting was cured by UV lamps immediately. The gel-like support material is jetted at the same time with model material, and can be removed mechanically after the part is completed. Most of the components of the implanter prototypes were manufactured by RP process, except needles, Teflon tube, springs, screws, and o-rings. Fig. 9 shows the assembled prototypes of three designs. Their implanting procedures of one cycle are demonstrated in Fig. 10-12.

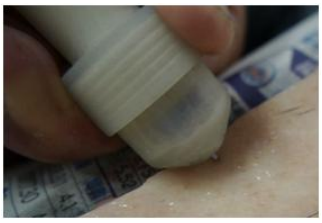
(a) auto-expand type implanter

(b) bar-cartridge type implanter



(c) rotary-cartridge type implanter

Fig. 9 Assembled prototypes of three implanter designs



(a) pierce the derma

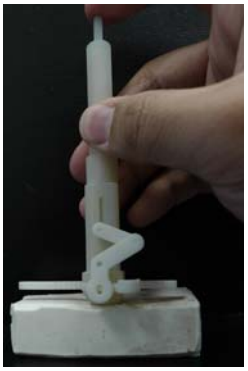
(b) expand the pierced hole

(c) push out the implant

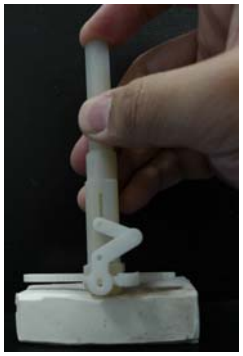
(d) cut off the gel and return

Fig. 10 Implanting procedure of auto-expand type implanter

(a) pierce the derma



(b) move cartridge for alignment



(c) push out the implant

(d) release and return

Fig. 11 Implanting procedure of bar-cartridge type implanter

(a) pierce

(b) push out implant

(c) release

Fig. 12 Implanting procedure of rotary-cartridge type implanter

IV. TESTING AND COMPARISON

A. Efficiency Comparison

Implanter's efficiency is related to its future clinic practices. The assembly time before implantation and the cartridge exchange time are listed in Table 2 for the three designs. Besides, the time spent in implanting 100 units was simulated on a foam pad. Since the maximum capacity of each design (28 units for auto-expand type, 21 units for bar-cartridge type, and 45 units for rotary-type) is different, numbers of cartridge exchange may vary accordingly. To implant 100 units, the auto-expand type needs to exchange loading tubes 3 times, while the bar-cartridge type needs to exchange cartridge 4 times and rotary-cartridge type needs to exchange 2 times. The total implantation times of 100 units are also shown in Table 2. It is obvious that bar-cartridge type implanter has advantages over the other two

in assembly and cartridge exchange, resulting in better operational efficiency in implanting 100 units or more, which is usually the case in the clinical practice.

TABLE 2 Time comparisons

	auto-expand type	**bar-cartridge type**	**rotary-cartridge type**
Assembly	1 min 24 sec	1 min 12 sec	1 min 52 sec
Cartridge exchange	42 sec	3 sec	27 sec
100-unit implantation	4 min 51 sec	2 min 44 sec	3 min 30 sec

B. Simulated Implanted Results

In addition to the preliminary test in the previous section, a simulated implanting test was also conducted by using the dyed agar to simulate cells aggregates implanting into porcine derma. Because the auto-expand type implant had a problem of implant accumulation and block the needle tip, only bar-cartridge type and rotary-cartridge type were tested in the experiments. Two combinations of needles described in section II were also investigated. The implanted biopsy samples were observed by a microscope. Ten times of implantation were tested to evaluate the successful rate with and without a pre-cut on porcine derma before implantation. Since the depth of a pre-cut is hard to control precisely, only the implanted depth of direct implantation without a pre-cut was measured. The results are listed in Table 3 and 4.

TABLE 3 Simulated implantation successful rate

			Successful Rate
Bar-cartridge type	fine needles	no pre-cut	90%
		pre-cut	100%
	thick needles	no pre-cut	90%
		pre-cut	100%
Rotary-cartridge type	fine needles	no pre-cut	60%
		pre-cut	70%
	thick needles	no pre-cut	90%
		pre-cut	100%

TABLE 4 Simulated implanted depth without a pre-cut

		Implanted Depth (mm)	
		Average	**Standard Deviation**
Bar-cartridge type	fine needles	1.03	0.40
	thick needles	1.03	0.35
Rotary-cartridge type	fine needles	0.54	0.21
	thick needles	1.98	0.23

A pre-cut is helpful on successful rate, especially for the rotary type implanter. Thick needles combination implants larger amount with better successful rate, but the scar is expected to be bigger. The fine needles combination is more difficult to push the implant through the fine needles, resulting in less successful rate in the test. For the bar-cartridge type implanter, the influences of needle size on successful rate and implanted depth are not obvious, while the rotary-cartridge type showed great differences.

C. Discussions

From the results of implanting efficiency, successful rate, and implanted depth, bar-cartridge type implanter is more suitable than the other two types. If we look into operation and control characteristics, rotary-cartridge type has several merits on stable holding, one step less than the others to complete the implantation, ease of applying force, less vision block during implanting, and no pressure applied to the skin. However, the alignment of the bar-cartridge type is better. The total weight of bar-cartridge type is the least, while the rotary-cartridge type is the most. Therefore, for overall consideration, bar-cartridge type implanter is the best choice among three.

V. CONCLUSIONS

In this research, three types of continuous implanters for DP cells aggregates were developed. With the adoption of RP technology, we could generate prototypes of the implanters for implantation simulations. Efficiency and implanted depth were specifically evaluated. The results revealed that the bar-cartridge type implanter had the best performance and highest speed among the three, and is considered the most feasible and suitable design to continuously implant DP cells aggregates.

REFERENCES

[1] T. H. Young, C. Y. Lee, H. C. Chiu, C. J. Hsu, S. J. Lin, "Self-Assembly of Dermal Papilla Cells into Inductive Spheroidal Microtissues on Poly(Ethylene-Co-Vinyl Alcohol) Membranes for Hair Follicle Regeneration," *Biomaterials*, 29(26) (2008) 3521-3530.

[2] Y. C. Choi, J. C. Kim, "Single Hair Transplantation Using the Choi Hair Transplanter," *Journal of Dermatologic Surgery & Oncology* , 18(11) (1992) 945-948.

[3] P. Boudjema, S. Boolauck, "Automated Hair Transplant System: The Boudjema technique," *Hair R eplacement: Surgical and Medical*, Mosby Elsevier Health Science (1996) 370-375.

[4] S. J. Lee, H. J. Lee, S. J. Hwang, D. W. Kim, J. B. Jun, S. L. Chung, J. C. Kim, "Evaluation of Survival Rate after Follicular Unit Transplantation Using the Knu Implanter," *Dermatologic Surgery* , 27(8) (2001) 716-720.

[5] W. R. Rassman, R. M. Bernstein, "Rapid Fire Hair Implanter Carousel. A New Surgical Instrument for the Automation of Hair Transplantation," *Dermatologic Surgery*, 24(6) (1998) 623-627.

[6] J. A. O'Brien, S. C. Lummis, "Diolistics: Incorporating Fluorescent Dyes into Biological Samples Using a Gene Gun," *Trends Biotechnology*, 25(11) (2007) 530-534.

[7] S. Bennett, C. Potter, "Pushing the Boundaries of Needle-Free Injection," *Drug Delivery Report*, (2006) 24-27.

[8] Zeranol Ralgro, (http://www.ralgro.com/)