Topical Pharmaceutical Application Device for Scalp

December 8th, 2010

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Abstract

Both chemotherapy drugs and radiation reduce tumor size by targeting and destroying rapidly dividing cells, including stem cells within hair follicles, which often causes a characteristic hair loss (alopecia). The pharmaceutical company Procertus has developed a drug, ProDermaCel, to help prevent alopecia in cancer patients. The company is ready to perform clinical trials with human subjects, but needs a new device to apply the drugs to a patient's scalp. The current proposed device consists of a L'Oreal hair dye comb attached to a MADomizer spray applicator using a rubber stopper. However, the current device may not pass standards set by the Institutional Review Board (IRB) because it appears unprofessional and the rubber elements could cause allergic reactions. Additionally, each applicator is expensive since the L'Oreal combs cannot be purchased independently of the hair dye kits. To overcome these issues, our group designed an application kit containing a hollow, linearly branching comb (figure 13), a 20 mL MADomizer spray applicator, 2 mL worth of drug dissolved in a 70% ethanol solution, and an FDA approved dye (FD&C Yellow #6 or Green #3). This new design appears professional and evenly dispenses the drug solution, with an average dead space of 0.68 mL and an average flow variation of 0.034mL between teeth. The device is comfortable for both the nurse and patient, and the nurse can apply the solution in an average of 38.0 s using this device. Further work for the project includes deciding on a large scale fabrication method and ensuring the connection between the comb and the spray applicator is secure.

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Introduction

Background and Motivation

Two of today's most common cancer treatments are radiation therapy and chemotherapy. Throughout the course of treatment, approximately half of all cancer patients receive some form of radiation therapy, which uses high energy x-rays, gamma rays, and charged particles to shrink tumors and destroy cancer cells [1]. Radiation is administered to the patient using an external machine or a radioactive substance injected into the body in the vicinity of cancerous cells [1]. Radiation destroys cancerous cells by damaging their DNA, killing the rapidly reproducing cells before they can repair the damage. Chemotherapy similarly destroys cancerous cells by damaging their DNA, but chemotherapy uses intravenously delivered drugs rather than radiation [2].

However, damage inflicted by chemotherapy and radiation is not restricted to cancerous cells. These therapies affect other rapidly dividing cells, most notably those of the GI tract, hair follicles, and bone marrow. As radiation or chemotherapy drugs damage follicular stem cells, the hair follicles stop functioning near the base of the hair shaft, which causes the hair to become weak and break as a result of everyday stress [3]. The beginning stages of alopecia (hair loss) can be seen in figure 1. In two recent "quality of life studies" patients ranked alopecia as the most noticeable side effect of cancer treatment [3]. There is currently no treatment on the market to prevent radiation or chemically induced hair loss. Doctors often encourage patients to buy wigs before starting therapy, but these wigs are usually expensive and not always covered by the patient's insurance plan [4].

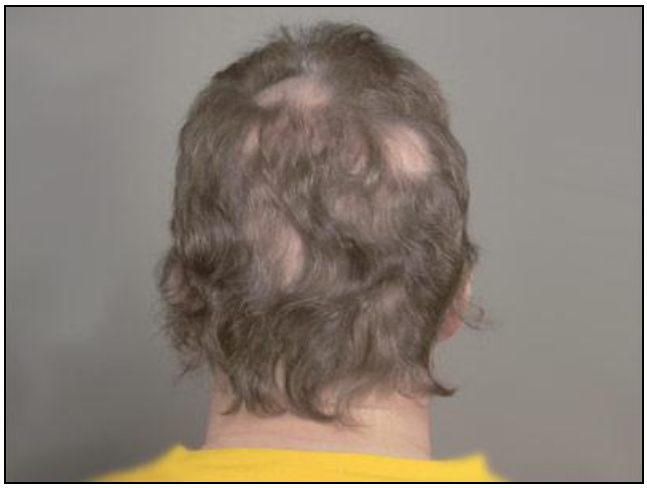

Figure 1: Image of hair loss due to chemotherapy [4].

Procertus is an oncology based biopharmaceutical company, attempting to develop drugs that alleviate the side effects of radiation and chemotherapy for cancer patients. The company has developed a drug called ProDermaCel to prevent alopecia in cancer patients receiving radiation or chemotherapy [3]. Initial testing in mouse models has shown that ProDermaCel can effectively prevent alopecia due to radiation therapy (figure 2). Procertus has planned clinical trials of the drug for human subjects in upcoming months and needs a drug application system that complies with IRB protocols for human testing.

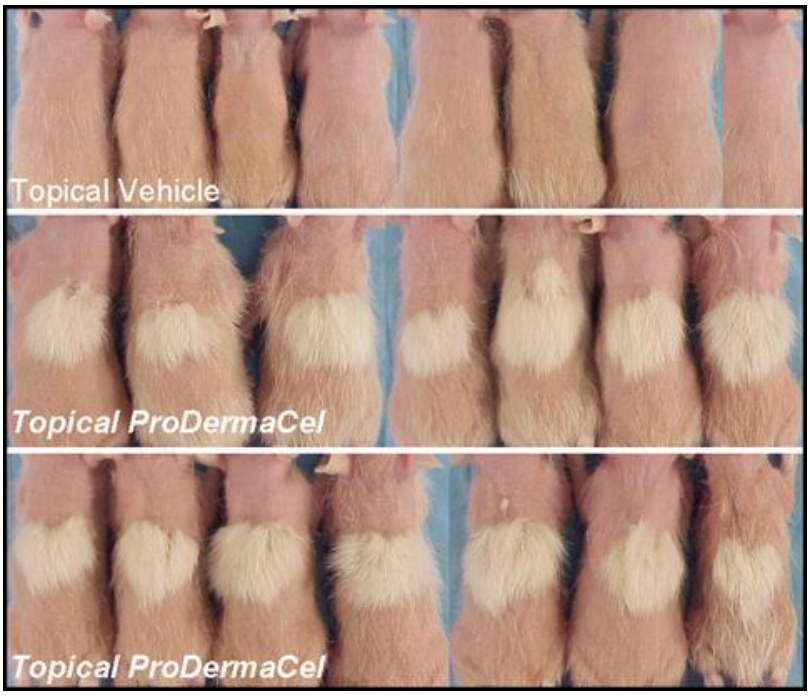

Figure 2: Images of initial testing using ProDermaCel in mouse models receiving radiation therapy. The drug effectively prevented hair loss in early trials [3].

Current Device

The current device, as proposed by Procertus for use in humans, is specific to the company's purpose, because there are no completely compatible designs on the market. The company has developed its own rudimentary device, which consists of a hollow L'Oreal hair dye comb attached to a 20 mL MADomizer spray applicator from Wolfe Tory Medical, Inc. The comb is attached to the spray applicator with a common rubber stopper (figure 3).

Figure 3: Current device consisting of a hollow L'Oreal hair dye comb attached to a MADomizer spray applicator from Wolfe Tory Medical using a rubber stopper.

This device delivers 2 mL of drug solution with 70% ethanol, 30% water to a 50 cm^2 area of the patient's scalp at a rate of 0.1 mL per spray. However, this device is cumbersome, contains an excessive amount of dead space, and appears unprofessional. Additionally, the rubber elements could cause allergic reactions in patients, and the comb tip is expensive because the combs cannot be purchased independently of L'Oreal hair dye kits, which cost upwards of $9.99 per package. These issues diminish the chances of the IRB approving the device for clinical trials. The client desires a new disposable device that will cleanly, comfortably, and accurately dispense the drug solution onto a patient's scalp.

Design Criteria

The design should address the following points: application should be clean and accurate, quick and comfortable, and safe for the patient.

Firstly, the device should cleanly and accurately apply the drug solution to a patient's scalp. The applicator must deliver 2.0 mL ± 5% of a drug solution containing 70% ethanol, 30% water to a 50 cm^2 area of the patient's scalp. The device should minimize the amount of drug wasted on the patient's hair and limit dead space in the device to 1.0 mL.

The drug will be applied by a certified research assistant (CRA), who should be able to use the device to quickly and comfortably apply the drug. The CRA should be able to apply the drug within a 60 to 90 s time span. The device should weigh less than 0.5 kg when filled, to allow the CRA to hold and manipulate the device with minimal effort. Applying the drug should not cause the CRA discomfort even after repeated applications.

The applicator must be safe and comfortable for patients. This means that the comb tip must still be comfortable against a patient's sensitive, irradiated skin after multiple applications. Additionally, the materials used in the device should be compatible with the water and ethanol solution, to prevent the leaching of harmful chemicals into the solution. To prevent cross contamination, the device should be one time use and should not contain natural latex due to potential patient allergies. The device must conform to the IRB standards for clinical trials with human subjects.

Lastly, the shelf life of the final product should be between 3 to 6 months, to span the time of the trials, which will take between 1 to 2 months. The 3 to 6 month time span allows ample time to complete the studies without having concern for the device's expiration date. Though only one prototype is needed, ideally 300 to 400 devices would be made to cover the trials, which include 12 patients with 25 to 35 applications each. The budget for the project is $300 to $400.

Overview of Design Alternatives

Our group decided to divide our design into two different components: applicator comb tips and applicator reservoirs. The two components were evaluated separately, and the best option from each contributes to our final design.

Applicator Reservoir Designs

Spray Bottle Reservoir

Our client currently uses a MADomizer spray bottle reservoir from Wolfe Tory Medical (figure 4). The bottle consists of a glass vial to hold the solution and a trigger component, which is screwed onto the bottle and can be easily removed to fill the glass vial. The comb component is attached where the liquid is released. The solution is dispensed by pushing the trigger. We could use the Wolfe Tory Medical, Inc. MADomizer that our client currently uses or research other options. Either way, this reservoir would be purchased, rather than fabricated by the team.

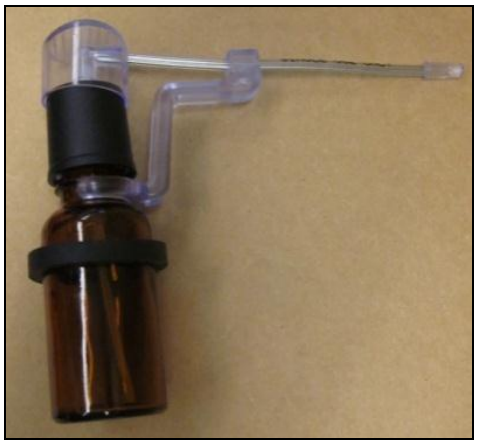

Figure 4: A 20 mL MADomizer spray applicator from Wolfe Tory Medical.

Syringe Reservoir

The syringe reservoir is a typical syringe with a male Luer-Lok connection fitting at the tip (figure 5). This is a standardized taper for syringes that allows for a variety of attachments, since it is compatible with any fitting equipped with a female Luer-Lok taper [5]. The comb component of our design would have the female Luer-Lok taper so it could be easily screwed onto the tip of a syringe. The solution is drawn up into the syringe before attaching the comb, and the solution is then dispensed by depressing the syringe plunger. The syringe reservoir would also be purchased by the team.

Figure 5: A commercially manufactured 10 mL syringe with a Luer-Lok tip [6].

Hollow Reservoir with Solution Ampoule (small glass vial)

The hollow reservoir is based on the ChloraPrep Frepp Applicator (figure 6). As with the Frepp applicator, our design would contain the drug solution in an ampoule, or small glass vial, located inside the plastic reservoir. With the Frepp applicator, the user breaks the ampoule by squeezing a side arm on the outside of the handle to release the solution. Our design would use a similar principle, with a modified ampoule and side arm. The comb attaches to the tip of the reservoir. Flow of the solution is controlled primarily by gravity; however, a hole in the side of the reservoir allows the CRA to stop and restart the flow by covering the hole with his/her finger. This hole is not necessary for the Frepp applicator because the sponge at the tip of it provides resistance against the liquid flow, while our comb would not provide significant resistance. The hollow reservoir would be fabricated by the team.

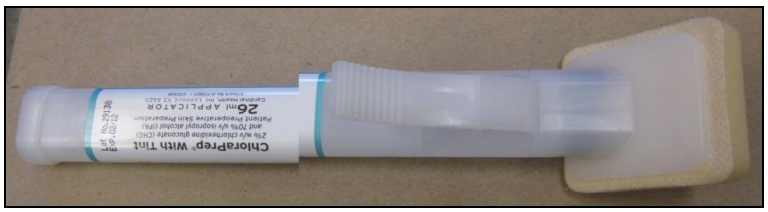

Figure 6: ChloraPrep Frepp Applicator, containing drug solution within a small glass vial that can be broken using the side arm to dispense the drug solution.

Evaluation of Applicator Reservoir Design Alternatives

In order to choose the final design, a design matrix was created that rated each reservoir design alternative on seven criteria: amount of control over liquid, amount of dead space, preparation time, liquid storage, administrator comfort, cost, and test results. More weight was given to more important criteria (table 1).

Table 1: Design matrix for reservoir design alternatives. Based on a series of weighted qualities the syringe option is best for our goals.

Criteria	Spray Bottle	Hollow with Solution Ampoule	Syringe
Amount of Control over Liquid (30)	27	20	26
Amount of Dead Space (20)	14	17	19
Preparation Time (15)	9	15	11
Liquid Storage (15)	12	15	9
Administrator Comfort (10)	7	9	6
Cost (5)	3	1	4
Test Results (5)	2	1	4
TOTAL (100)	**74**	**78**	**79**

The amount of control over liquid rating reflects the degree that the CRA can control how much solution is dispensed. This category was weighted the most because during the application process, a specific amount of solution must be applied to a specific area of scalp, and the more control the CRA has over the amount of liquid that is dispensed, the more evenly the liquid can be applied to the area. The spray bottle would give the administrator the most control because each spray is a consistent volume of liquid. In the case of the MADomizer, our client measured that each spray is 0.1 mL. The syringe would have a decent amount of control because the CRA can control how fast or slow he or she pushes the plunger in, thereby controlling how much liquid is dispensed. Due to human error, however, the amount dispensed would not be consistent throughout the application procedure, but we decided that this lack of consistence would not be too great to compromise the effect of the drug. The hollow reservoir would give the least amount of control over solution flow because it is primarily controlled by gravity and the hole on the side of the reservoir would basically provide the minimal control of an on/off switch.

The amount of dead space rating reflects the amount of solution that is not dispensed on the scalp because it is "stuck" in the reservoir. This category was given more weight because it is important that we minimize the amount of wasted drug solution to minimize cost, since the drug is expensive. The syringe would have virtually no dead space since the plunger can be pushed all the way to the bottom of the syringe, dispensing all of the solution. The hollow reservoir might have some dead space because solution might get trapped at the bottom of the reservoir due to the fact that there is nothing forcing the tiny remaining volume of liquid into the comb. The spray bottle would have a significant amount of dead space because the tube of the spray bottle has to be filled with liquid before any is actually dispensed. Our client informed us that the MADomizer has about 1 mL of dead space.

The preparation time rating reflects how long it would take the CRA to prepare the device before starting the application process. This category was weighted in the middle because it is important that we take time into account, but it is not the primary focus of our design. The hollow reservoir would have the quickest preparation time. The solution is stored in the reservoir, so the ampoule just has to be broken before application can begin, and this is a quick process. With the syringe, liquid would have to first be drawn up into the syringe which would take a little longer. The comb would have to be screwed on, but due to the Luer-Lok tapering, this would be a quick process. Liquid would have to be poured into the spray bottle, which takes time because the CRA has to be cautious that solution is not spilled in the process. The trigger component would also have to be screwed on.

The liquid storage rating refers to the location and method of solution storage. This category was also weighted in the middle because it is important to take it into account, but it is not the primary focus. The hollow reservoir has the best and most convenient method for liquid storage because the solution is stored in a glass ampoule incorporated within the design. The location of the solution for both the spray bottle and syringe would be in an external glass container. Since the syringe is made of plastic, some issues could result because the solution's properties could be compromised if it comes in contact with plastic. This is why it was rated below the spray bottle. However, it is not too big of a concern because the solution would not be in the syringe for a prolonged period of time, and our client did not express any concerns about this when we discussed our ideas with him.

The administrator comfort rating refers to the how much strain the method of dispensing the liquid would put on the CRA. This category was not given much weight because it is something to consider but is not the focus of our design. The hollow reservoir would give the CRA the most comfort because gripping the reservoir while having a finger over the hole would not put a significant amount of strain on his or her hand. The spray bottle would be a little less comfortable because the CRA must continuously push the trigger, and this repetitive motion could cause some strain. The syringe would be the least comfortable because the administrator must be conscious of controlling his or her motion while simultaneously pushing the plunger in. This motion over a certain period of time could be straining.

The cost of the device was not an important factor in our decision. Any patient receiving radiotherapy will be spending a considerable amount of money on this procedure, so the cost of our device in this process will seem minimal. Our client also gave us a flexible budget between $300 and $400. The hollow reservoir would cost more in both time and money than the spray bottle and the syringe because it would have to be fabricated by the team. The spray bottle might cost a little more than the syringe due to the amount of solution that would be wasted on dead space in the device.

The test results rating refers to preliminary tests that were conducted on our design ideas, as explained in the testing section on page 12. This category was an end-determining category for our design alternatives and was not given much weight because our testing was based primarily on qualitative observations. An explanation of the results of this testing can be found in the Testing section. Based on this testing, the syringe was ranked the highest in this category.

Applicator Comb Tip Designs

Straight Comb

The straight comb tip consists of one main horizontal tube. One end of this tube is equipped to connect to the reservoir and this location is where the drug solution enters the comb. The other end of the main tube has eight vertical tubes extending out to form the comb teeth, as shown in figure 7. The ends of the eight teeth are the exit pathways for the solution to deliver the drug directly to the scalp. These eight teeth would be either curved to better fit the contour of the scalp or be made out of a pliable material so as to ensure patient comfort.

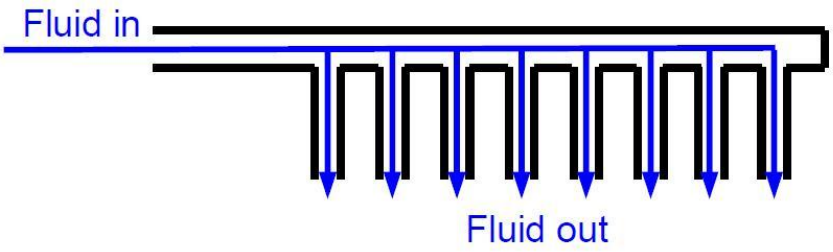

Figure 7: The straight comb tip, with the flow of the drug solution shown in blue.

Angular Branches

The angular branched tip starts with one vertical, short tube that will be the entrance point of the drug solution and will connect to the reservoir. This vertical tube immediately branches into two angled pathways. Further down, each of these pathways has one tube branch off internally to form a total of four pathways, as shown in figure 8. This angled branching continues until there are eight total pathways; the ends of which are the teeth of the comb tip. This tip will use the same method as the straight tip to ensure that the comb is comfortable for the patient by utilizing either a contoured shape or a pliable plastic.

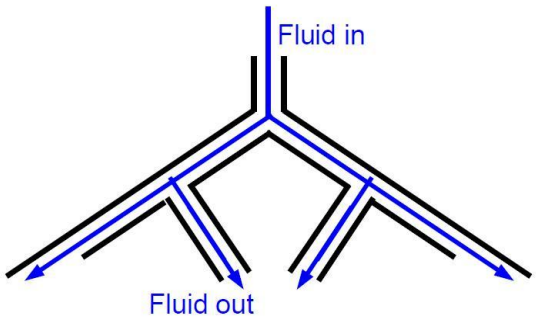

Figure 8: The angled branch comb, with the flow of the drug solution shown in blue.

Linear Branches

The linear branched comb tip would be a similar alternative to the angular branched tip. The significant difference is that all the tubing and branches have 90° turns, making all the tubes either vertical or horizontal in position. Each vertical tube in the tip branches into two horizontal tubes until the end of the tip has eight vertical tubes that act as the teeth of the comb, as shown in figure 9. The ninety degree angles provide equal resistance in every pathway of the comb which is unique to this specific tip. Just as the other two design alternatives, this comb utilizes either a contour shape or pliable plastic for patient comfort.

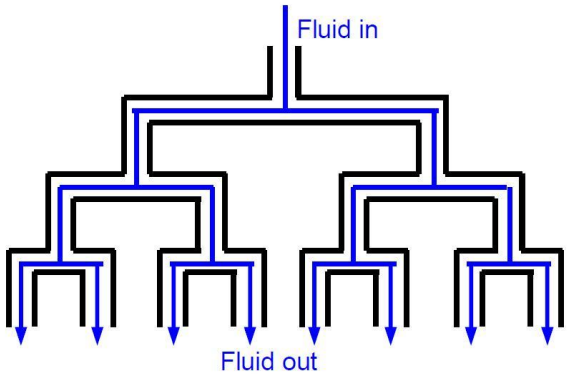

Figure 9: The linear branched tip, with flow of the drug solution shown in blue.

Evaluation of Comb Tip Design Alternatives

A design matrix was created to aid in making the decision between the three alternative tip designs. The matrix was weighted on six different criteria, with the client's most important criteria being more heavily weighted. The criteria from heaviest to least amount of weight are as follows: application accuracy/cleanliness/even distribution, ease of use through hair/speed of attachment, patient comfort, amount of dead space, feasibility, and cost (table 2).

Table 2: Design matrix for applicator comb tip: the matrix indicates that the comb with the linear branch design is most effective for this project.

Criteria	Straight	Linear Branches	Angled Branches
Application Accuracy, Cleanliness, and Even Distribution (30)	19	28	23
Ease of Use Through Hair (20)	18	15	14
Patient Comfort (20)	17	16	16
Amount of Dead Space (15)	11	10	13
Feasibility (10)	9	7	6
Cost (5)	4	4	4
TOTAL (100)	**78**	**80**	**76**

Application accuracy/cleanliness/even distribution was the criterion that was most heavily weighted because of its extreme importance to the client. The device tip must ensure that the 2 mL of drug solution is applied to the 50 cm^2 area of scalp cleanly. To do this, the comb must have an even distribution of solution flow through all of the teeth in the comb. The linear branched comb received the highest score in this area because of its characteristic 90° angles. The 90° angles give each pathway an equal resistance which therefore ensures that the drug solution will be equally distributed to all the tubing and comb teeth. The angled branches tip received five points less because of the angles of its branches. Although some solution will reach every pathway, it is likely that most of the liquid will stay in the initial two branches. This will cause the flow of the solution to be unequally distributed with a heavier flow on the outer comb teeth. The straight comb received the lowest score of only nineteen because of a similar reason. The teeth that are closest to the to the solution entrance of the main tube will receive the most solution and less solution will be able to pass over the first teeth to reach those near the end of the tube giving the tip an uneven distribution and low accuracy.

The equipment required for radiation therapy is very expensive; therefore clinics tend to pass patients through quickly to ensure they see as many patients as possible. Thus, our device should minimize application time for the drug solution, to avoid adding excess time to the radiation process. The comb tip must there for be easy to attach to the reservoir and easy to use. For this reason, speed and ease of use are the next highest criterion in weight. Ideally the comb applicator will pass clinical trials and be used on patients whose hair is longer than 25.4 mm, so the tip must easily comb through all hair lengths. The straight comb received the highest score in this area because of the stability that the main tube gives the teeth. This stability makes it easier to comb through the hair and get the ends of the comb teeth directly on the scalp for application. The linear branched comb received three less points because it has nothing to give the teeth the same kind of stability. Less stability implies that the comb will not brush through hair as well, and some drug could potentially be lost to the hair. The angled comb received one point less than the linear branched comb because its angled branches are slightly less stable and rigid than the 90° branches are for the linear comb.

Patients undergoing radiation therapy can have very sensitive skin where the radiation occurs. Because the comb tip will be directly in contact with this sensitive tissue, it is very important that the comb is comfortable for the patient. All three comb tip designs have the potential to be contoured or be made of a more flexible material to ensure patient comfort. Based on the tip alone, the straight comb received the highest. The higher score here also has to do with the support of the main tube of the design. The main tube is directly connected to the reservoir and lack of branches could potentially make it slightly easier for the clinical assistant to control and gauge the pressure they are using to comb through the hair. This would make the combing process slightly more comfortable for the patient than the two branched combs; however, this is the only small advantage that the straight comb has in this area.

The next most important criterion is the dead space in the tip. The drug is expensive so its waste must be minimized. Dead space in a device is tubing or area that must be filled with drug solution before the drug solution will start exiting the comb to be applied to the scalp. The angled branch tip received the highest score in this area due to its lack of horizontal tubing, which allows all but a small portion of the solution inside of the tubing to exit the comb due to gravity. The straight tip earned two points less than this because its main tube is horizontal and theoretically the portion of the tube before the teeth start extending off would still contain solution in it. The linear branched tip received the lowest score because it has seven horizontal tubes in total that would all contain remaining liquid.

Feasibility of the design was also considered in the matrix, referring to the ease of fabricating the device. The straight comb earned a higher score because of the simplicity of the design. There are no branches or horizontal fanning in this tip, which makes it the easiest to fabricate. However, SolidWorks models and rapid prototyping companies make the two branched tips as slightly more complicated but

equally feasible alternatives. The horizontal and vertical positioning of the linear tip makes it only slightly less complicated than the angled branches tip but enough to cause it to gain an extra point in the feasibility criterion of the matrix.

The last and least weighted criterion taken into consideration was the cost of the tip. All three tip design alternatives would involve rapid prototyping for fabrication and since the client gave us a flexible budget for the project, all three designs received the same score for cost.

Initial Testing

To get the best idea of which design alternatives would be the best to pursue, the team created a crude branching comb for attachment to the different reservoir types. Based on fluid dynamic information from Professor Naomi Chesler, we decided to make a branched comb with forks that split evenly, such as a Y- or T- connector. Such a design will theoretically produce the most even distribution of flow. Materials were purchased from an online supplier (amazon.com®), and include plastic medical tubing [both 2.38 mm (3/32 in) and 0.794 mm (1/32 in) inner diameters], white nylon Y-connectors [2.38 mm (3/32 in) inner diameter], and rubber cement. A cost table for these materials can be found in the appendix in table 8. These materials were assembled to create a branching comb that began as one channel and branched into eight, as shown in figure 10.

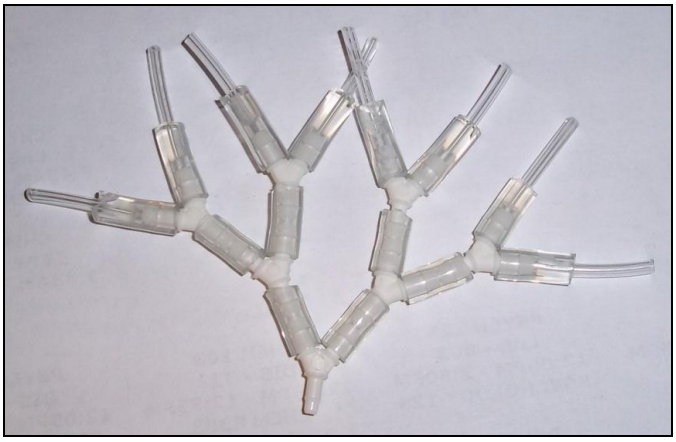

Figure 10: Prototype for the branching comb as used in preliminary testing.

This comb was attached to each reservoir type indicated in the design alternatives: the syringe, the spray bottle, and the hollow reservoir with a glass ampoule. Each reservoir type was used to dispense a volume of water and was judged qualitatively on the amount of control of flow, the comfort for the user, and the ease of preparation. Based on these criteria, the syringe was determined to be the most effective out of the three. The syringe offered the greatest control over the flow of liquid, it was easy to stop and restart the flow of water. Holding the syringe was also moderately comfortable during the dispensing of liquid, and it could potentially be improved by adding a handle to make it more ergonomic. Furthermore, the syringe was easy to prepare; the process involved drawing up a volume of water without the comb attached, and then putting the comb tip on, and then it was ready to dispense water.

The spray bottle and the hollow reservoir were less effective. Although the spray bottle performed well in amount of control over liquid flow, it was slightly less comfortable to use because we had to squeeze the trigger repeatedly before liquid was sprayed. It also took slightly longer to prepare the spray bottle because it had to be opened to pour in the water and then closed again. The water also did not immediately come out of the tip because it took a number of squeezes to fill the dead space. A crude model of the hollow, gravity-driven applicator was created by poking a small hole near the top of

a syringe and controlling the flow of liquid by controlling the air flow through the hole instead of using the syringe plunger. Using this device, it was much harder to control the flow of liquid, and it was also less comfortable to hold because the air flow through the hole had to be carefully monitored to prevent all the liquid from rushing out. Although it would have a very easy preparation process, as simple as cracking a glow stick, this reservoir type just did not offer enough control.

The final preliminary test was to assess the evenness of fluid flow through each of the branches of the preliminary comb. This was accomplished by placing each branch opening into a separate collection tube to catch the water, as shown in figure 11. All eight branches were included, and approximately 4.5 mL of water was dispensed in total. The volumes of water were read from the graduations on the sides of the tubes. The data collected is shown in figure 12. Although the volume of water dispensed by each branch was not completely even (mean = 0.556 mL, standard deviation = 0.086 mL), it seems to be pretty even overall. The amount of variation is expected to decrease for a professionally manufactured comb, because this would eliminate some fluid resistance variability that is inherent in the crude design of the prototype comb.

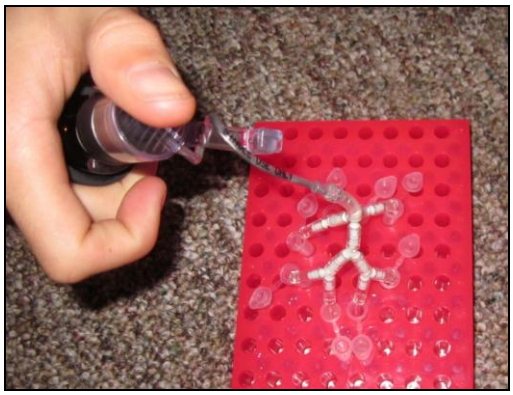

Figure 11: Shows the setup of the collection tubes used to test the evenness of fluid flow in the preliminary comb designs.

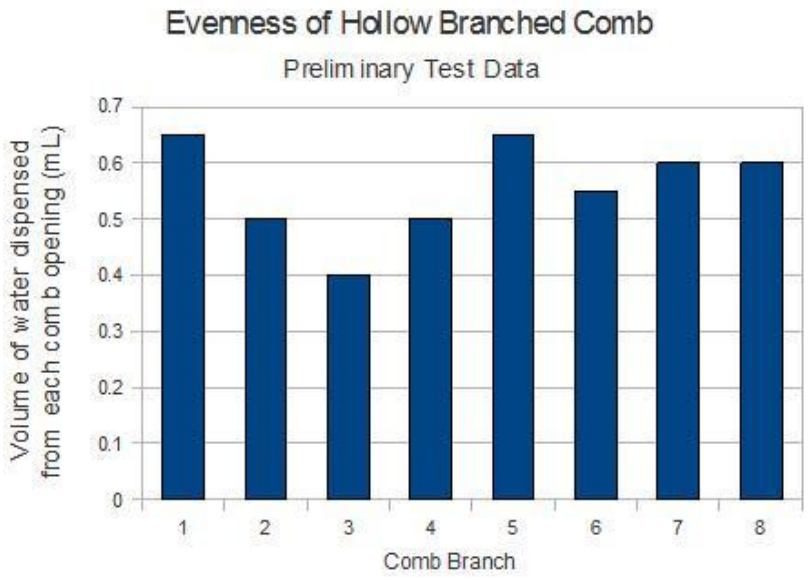

Figure 12: Data from evenness test shows that the flow from the prototype comb was generally even, but not perfect. With a professionally fabricated comb, it is expected that the distribution more equal because the fluid resistances in each branch will be closer to equal.

Final Design

Based on our design matrices and preliminary testing results, we had initially chosen to design a kit consisting of a syringe, a linear branching hollow comb tip, a vial of the pharmaceutical solution containing the active drug and an FDA approved dye, and a handle for the syringe. However, discussion with our client and further testing has led us to switch our final kit to use the MADomizer spray bottle instead of the syringe as the reservoir. The reason for this switch is that the MADomizer provides greater control over the amount of fluid dispensed, in that each squeeze of the spray bottle accurately delivers 0.1 mL of fluid. Furthermore, it was noted during testing that the pulsing of the spray bottle leads to a more even flow distribution through the comb teeth. More details about this testing can be found in the testing section. Thus, the final design is a kit that contains the MADomizer spray bottle loaded with the pharmaceutical solution with an FDA approved dye and the linearly branched hollow comb tip (figure 13). For long term storage of drug solution in the MADomizer bottle, the bottle can be alternatively capped with an inert cap instead of the plastic, fluid-dispensing spray cap.

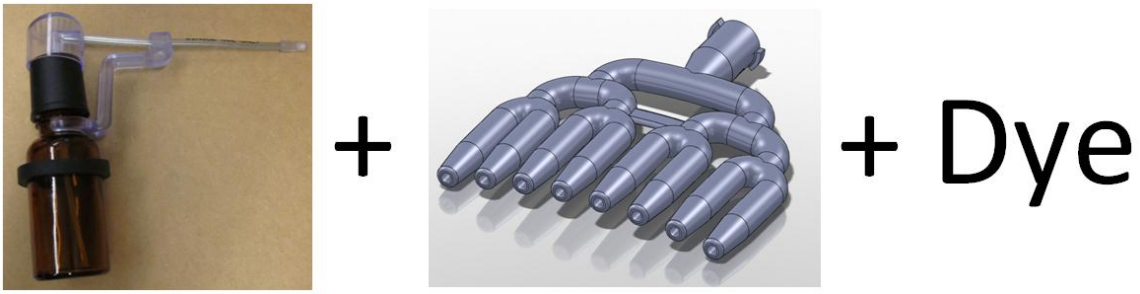

Figure 13: Contents for the final drug delivery kit include a 20 mL MADomizer spray applicator, a linear branched hollow comb tip, and an FDA approved dye (FD&C Yellow #6 or Green #3).

Using this kit, the application process would proceed as follows. The research assistant for clinical trials would open the kit, consisting of a MADomizer spray bottle capped for long term storage, the spray cap for the MADomizer, and the comb tip. After switching the inert cap for the spray cap, the research assistant would attach the comp tip to the end of the MADomizer. The research assistant would then use the MADomizer spray bottle to dispense all of the fluid onto the patient's scalp, taking the necessary time to comb through the hair and evenly spread the drug solution over the scalp, and thus completing the application process. The MADomizer and comb tip would then be discarded.

The main component of the kit that had to be designed was the linear branched hollow comb. This device was designed in SolidWorks and a digital drawing is shown in figure 14. The hollow comb has a number of key features. First of all, the branched design distributes the fluid relatively evenly out of each comb tooth. The comb is also flexed to fit the curvature of the scalp, using a radius of curvature of 75 mm. Furthermore, the end of the teeth are tapered and rounded to increase patient comfort. Finally, the attachment to the reservoir is designed to fit either the MADomizer spray bottle or a Luer-Lok syringe, increasing its versatility.

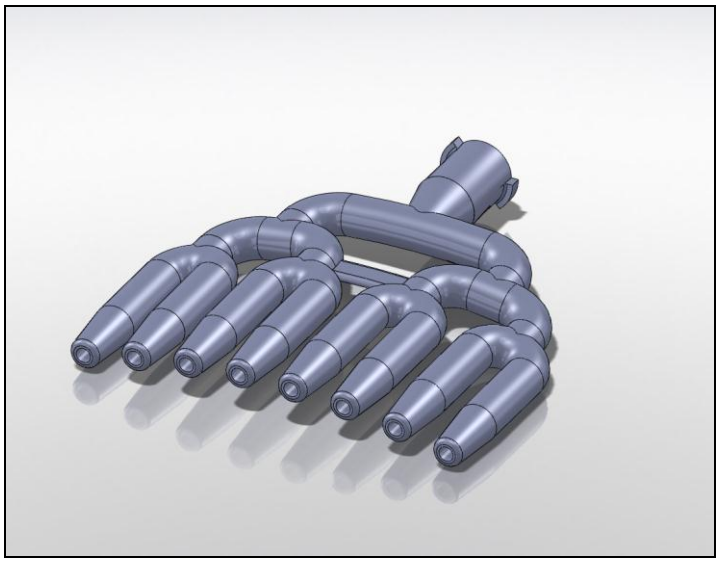

Figure 14: SolidWorks model for final comb.

Fabrication

SolidWorks Modeling

Using SolidWorks software our team developed a to-scale model for our device (figure 14). The specific dimensions for this model can be seen in figure 15.

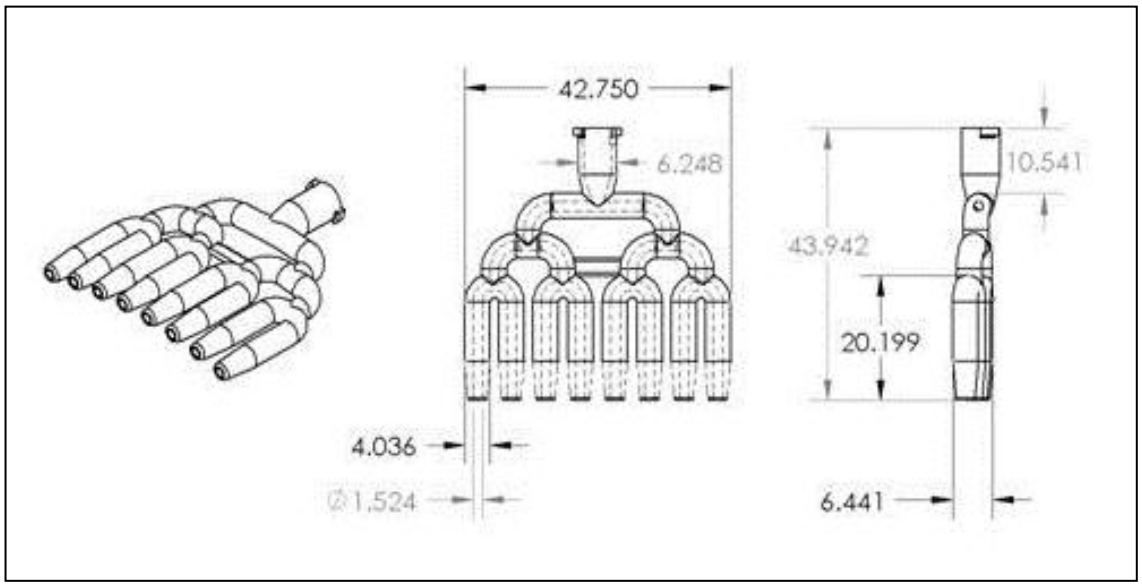

Figure 15: Dimensions for the final comb applicator tip (mm).

The comb tip attachment is compatible with a Luer-Lok syringe tip and the MADomizer spray applicator tip. The two wings found on the outside of the comb tip attachment correspond with the Luer-Lok thread dimensions shown in figure 16. The inside parameters match that of the MADomizer spray applicator tip, with a 4.81 mm larger diameter and a 4.45 mm smaller diameter (figure 17).

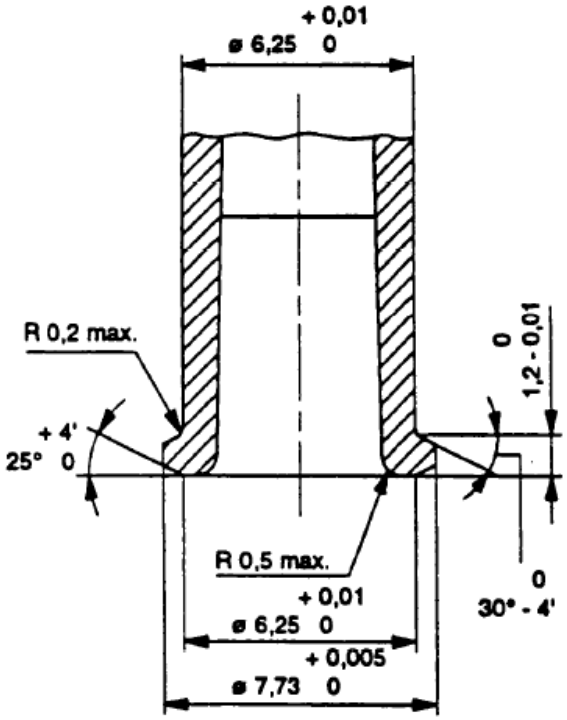

Figure 16: Schematics for a female Luer-Lok system with dimensions in mm [7].

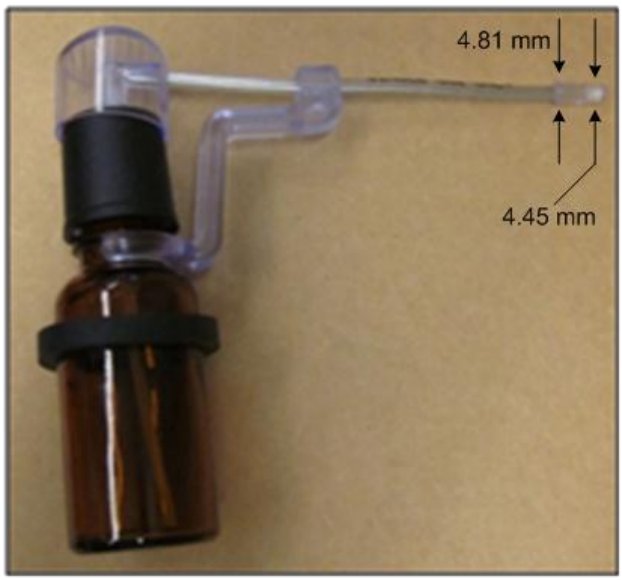

Figure 17: Shows dimensions of MADomizer tip compatible with the comb applicator tip

The SolidWorks model allowed our team to have a rapid prototype made for our part. This was done using fused deposition modeling (FDM) which works by laying down layer after layer of ABS plastic as guided by the SolidWorks model. This technique was used for an initial prototype, which was used during testing.

Recommendations for Fabrication

Direct Digital Manufacturing

One possibility for our client to obtain hundreds of copies of the hollow comb tip is to use direct digital manufacturing (DDM), or additive manufacturing, which refers to a process in which plastic parts are built up layer by layer using a printer-like machine (figure 18)[8]. In this process, the hollow tubes of the comb with be initially filled with a supportive material to allow for additional layers to be placed on top of them, but the supportive material can be dissolved to produce the necessary channels.

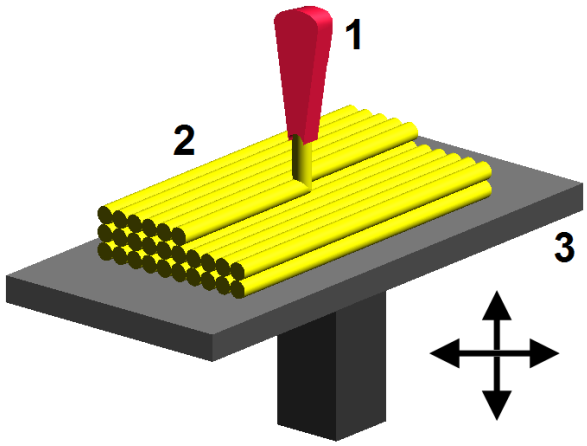

Figure 18: Fused deposition modeling (FDM), a method of rapid prototyping: 1 - nozzle ejecting molten material (plastic), 2 - deposited material (modeled part), 3 - controlled movable table [9].

There are a variety of concerns with using DDM to manufacture the comb tip. First of all, since the comb tip is very small, the layers of plastic must be small enough to give enough resolution to accurately construct the branched tubing structure. If the layers are not small enough, the channels may not be consistent, and may even be blocked in places. Resolution is also important to ensure that the teeth are tapered and rounded for patient comfort and that the reservoir attachment fits to the MADomizer and Luer-Lok tip. Another concern with DDM is that the choice of materials is limited. The comb tip needs to be rigid and strong so that it can part the hair and will not break during the application process. Additionally, it should not be so hard that it causes any discomfort to the patient.

There are many online companies that will use DDM to manufacture parts for customers, and most a digital file to specify the dimensions. To determine if these companies could feasibly manufacture the hollow comb tips for this project, we contacted a couple of them. One of these companies, RedEye [10], recommended that we use fused deposition modeling (FDM), a DDM process, to create our comb. RedEye is capable of using FDM with a layer thickness of 0.005 inches (0.127 mm), which they refer to as '.005" slice.' Based on a conversation with one of their representatives, they are confident that they can manufacture the hollow comb tip using the 0.005" slice FDM with ABS-M30 material, which is 25-70% stronger than standard ABS (Acrylonitrile/Butadiene/Styrene) [10], which was used to make the initial prototypes for testing. When asked for a quote for a single hollow comb device, they indicated that they would make one for $30. However, if we were to get hundreds of them manufactured the price per unit would be only $21. This seems to be a relatively high cost for such a small plastic part; thus, RedEye suggested that we use injection molding if we do not expect to make any changes in design, which would be a cheaper process. RedEye also indicated that they can assist us with injection molding if needed.

One last recommendation to our client with regards to direct digital manufacturing is to make sure the parts are satisfactory before ordering hundreds. In creating our rapid prototypes for testing, we used two different machines. In doing so, we noticed that they constructed comb teeth of slightly different inner diameters, a dimension that was exactly the same in the files we sent to the different printers. Being a commercial provider of DDM parts, RedEye should be able to create parts that match almost exactly the given dimensions, but it may be a good idea just to double check before ordering hundreds.

Injection Molding

Another way our client could obtain multiple comb tips is to use injection molding, a process in which thermoplastic is heated in a barrel and forced into a mold cavity where it is left to cool and harden into the shape of that mold cavity. This process is quick and the cost is minimal, only involving the costs associated with the type of plastic chosen for the part. The expensive part of the injection molding process is getting the specific mold fabricated. Molds must be fabricated by a mold-maker from a metal such as steel or aluminum and machined precisely to form the features of the specific part. An advantage of this process is that the part can be made from a variety of plastics, so our comb could be fabricated from a softer plastic that would be more comfortable on a patient's scalp. We would recommend using high density polyethylene as the material for the comb tip because we believe this material would be strong enough to comb through a patient's hair, but soft enough not to cause pain to an irradiated scalp.

There are many online companies that can make injection molds for customers. To determine if these companies could feasibly manufacture a mold for the hollow comb tip for this project, we contacted a couple of them. Only Engineering Industries, Inc. of Verona, Wisconsin responded. When we emailed them our SolidWorks file, they initially said that our part could not be made using injection molding. This is because our design involves undercutting. Undercuts are features on a part that will not allow it to slide out of the mold cavity in the machine [11]. In the case of our design, the undercuts are the branches of the comb. We emailed them again and asked if injection molding was possible if we molded our part in two separate halves that could then be welded together, and they responded with a solution.

First of all, they said that it is necessary to have some type of joint design that will provide positive alignment for the two halves when they are being welded together. Therefore, before injection molding could be done with our current design, it would have to be redrawn into two separate halves and have some type of tongue and groove joint design incorporated into it. After the design is modified, Engineering Industries, Inc. would be able to make a two-cavity family mold for our part. This type of mold would produce both halves of our part, which could then be welded together after molding. The estimated cost for a two-cavity family mold for our part is $20,000 [12]. This is probably more money than our client would like to spend to make 600-700 comb tips for clinical trials because the injection mold most likely would not pay for itself. However, if our client were to sell our comb commercially with his drug once it is FDA approved, injection molding might be a more feasible option for making the comb tips.

There are several different ways to weld the two plastic pieces together including ultrasonic, vibration and hot plate welding. These processes and their respective benefits are described in the following sections.

Ultrasonic Welding

Ultrasonic welding combines the two pieces together through vibrations. The two pieces are placed between a fixed anvil and a transducer extension and then exposed to a "very rapid, low-amplitude acoustic vibration" [13]. It takes less than a second for the acoustic energy to create friction and heat to weld the two pieces together. This type of welding is great for small pieces and since it is largely automated and requires no type of adhesive, it is a cost efficient welding process.

Vibration Welding

The vibration welding process is very similar to ultrasonic welding. The two pieces are vibrated/rubbed together at a predetermined pressure, frequency and amplitude. The friction caused by rubbing heats the contacting surfaces causing them to melt and combine. Once vibration ceases, the pieces cool and solidify into one solid part. Vibration welding is particularly useful for materials and plastics that are subject to thermo-oxidative degradation. However the vibration can prevent the two pieces from perfectly aligning and combining together, which could be very problematic for a small device like the comb tip [14].

Hot Plate Welding

Hot plate welding uses a thermally heated platen to join the two pieces together. The pieces are rigidly held and the heated platen is placed between the two. Once the connective areas of each piece reach a molten temperature, the platen is quickly removed and the pieces pushed together. They remain under pressure until the now welded part cools and can be removed from the holding mechanism. Hot plate welding can be used for very complex designs, including those that involve thin and non-supported interior walls [15].

Testing

Flow Analysis

SolidWorks FloXpress was used to initially analyze the flow through the comb tip. The flow rate was measured through each pathway as shown in figure 19. It was assumed that the flow rates would be similar in the left and right halves of the comb due to symmetry.

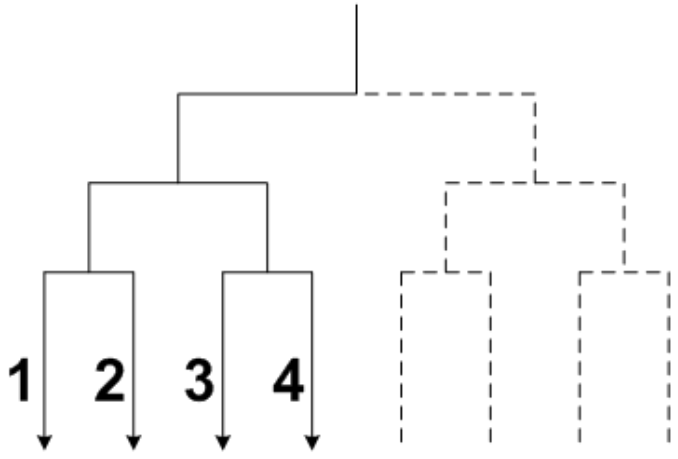

Figure 19: Labeled flow pathways through the comb.

The software analyzed the flow rate through each pathway with the input at the comb tip attachment. The flow rate into the comb was calculated using the initial testing data with the syringe attachment, which revealed that the average application time for the drug solution was 38 s. Subtracting the average 7 s for assembling the device that means the comb expelled 2 mL of fluid in 31 s. This turns out to be a flow of 0.065 mL/s. The flow calculations are shown in figure 20 below. The software then calculated the maximum flow rate through the pathway as shown in table 3 below.

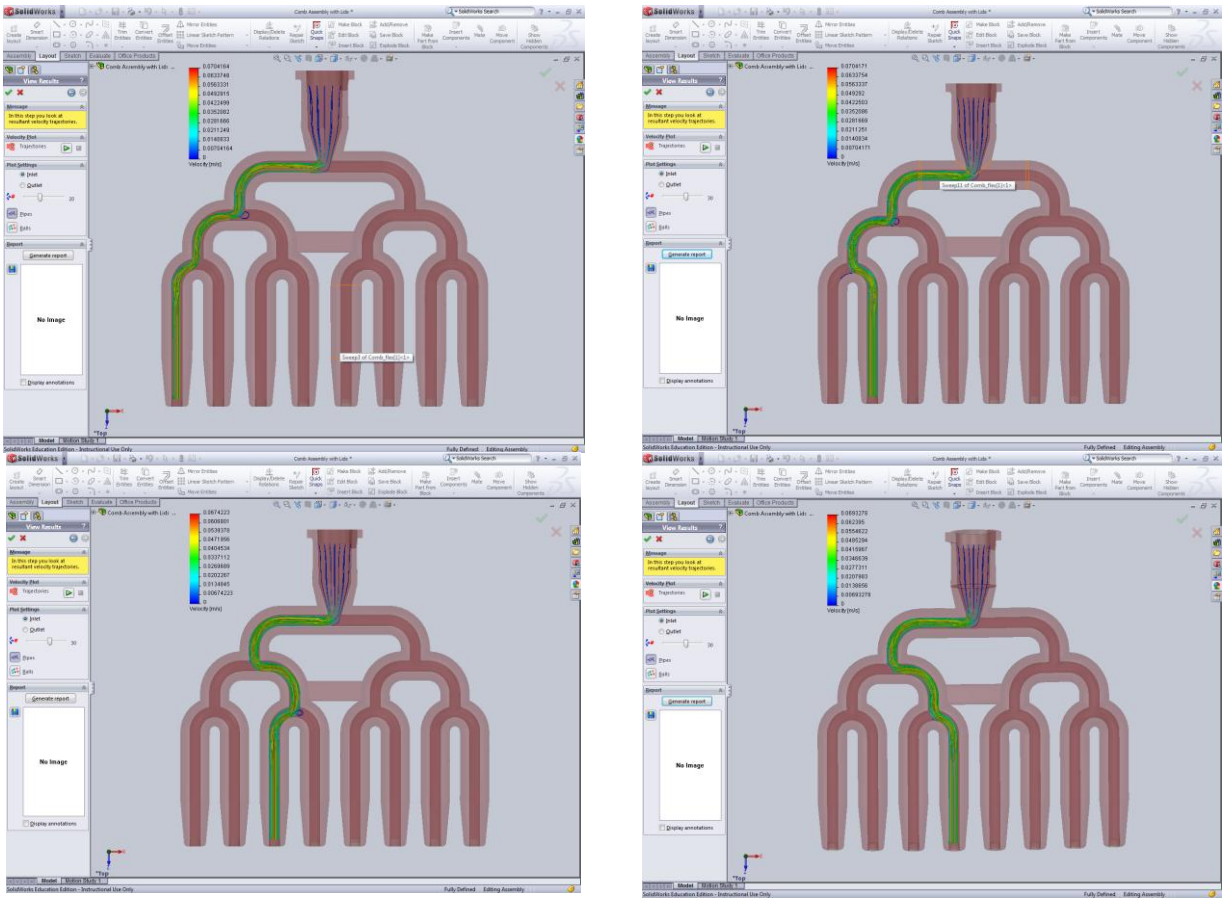

Figure 20: Flow through the different pathways

Table 3: Maximum flow velocity as determined by SolidWorks using FloXpress.

Pathway	Maximum Flow Velocity (m/s)
1	0.07022
2	0.07022
3	0.06741
4	0.06855

The analysis shows that the flow rate is slowest in pathway 3, followed by pathway 4, then paths 1 and 2. Since the pressure difference across each path was held constant in each simulation the flow rate is an indirect measure of the resistance for that pathway, using equation 1. This shows that the resistances in pathways 3 and 4 are highest and thus will receive slightly less flow. This is most likely due to the change in inertia that occurs at the second branch.

$$\Delta P = FR$$

Equation 1: Equation for pressure showing the inverse relationship between flow rate and resistance.

Field Testing

The team completed two set of tests this semester, one with the comb tip and the syringe and one with the modified comb tip and MADomizer. Testing with the syringe and comb tip as well as client input let us to modify the final design comb tip to be compatible with both a syringe and MADomizer. Complete testing data can be found in the appendix in tables 5-7. Testing with the syringe reservoir was conducted using a rapid prototype model of our comb tip, received from the biomedical engineering department's rented fused deposition modeling machine. Testing with the spray applicator was conducted using a second set of prototypes containing a slightly modified comb attachment compatible with the spray applicator tip. These prototypes were made also using fused deposition modeling, courtesy of Ahmed Khudair and Calix Networks.

We completed a test for dead space with the initial design of the comb tip and syringe because one of our design specifications, as requested by our client, was to minimize the amount of dead space in the device to less than a milliliter. This test was done by filling the syringe with 2 mL of a 70 % ethanol solution, attaching the comb tip, and then dispensing the liquid with the syringe into a small cup. The comb tip was then detached, the syringe plunger was pumped a few times to rid the syringe of excess solution, and the amount of solution in the cup was drawn up with the syringe and measured. This amount was then subtracted from 2 mL to calculate the amount of dead space. Eleven trials were conducted, and in each trial the dead space was significantly less than 1 mL with the average amount of dead space being 0.261 mL (figure 25).

Another test was done to measure the time it takes to apply 2 mL of water to a 50 cm^2 area of scalp, which are the parameters for application that our client gave us. This was done by cutting a 50 cm^2 square out of a piece of paper and holding this paper against a team member's scalp (figure 21). Another team member applied the water to this area of scalp using our device by squeezing the syringe and rubbing around in circles to spread the water around as would be done with the drug solution. Five trials were done and the average application time was 38 seconds. Graphical data for this test can be found in figure 22. A few qualitative observations were also made during this test. We found that a lot of fluid dripped down the scalp to the neck. This would be undesirable when applying the drug solution because it would waste solution and solution would be applied to areas it is not intended for. It was also difficult to judge how much solution was actually being applied to a certain area, since the dispensing process was not completely consistent, and we often found that there was an insufficient amount of fluid left toward the end to be applied to the final part of the scalp.

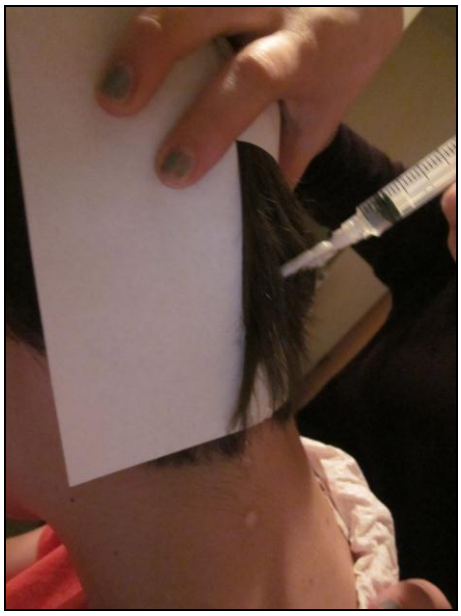

Figure 21: Setup for time trials with syringe and comb attachment. Time trials of application were done by applying 2.0 mL of water to a 50 cm^2 area on the scalp.

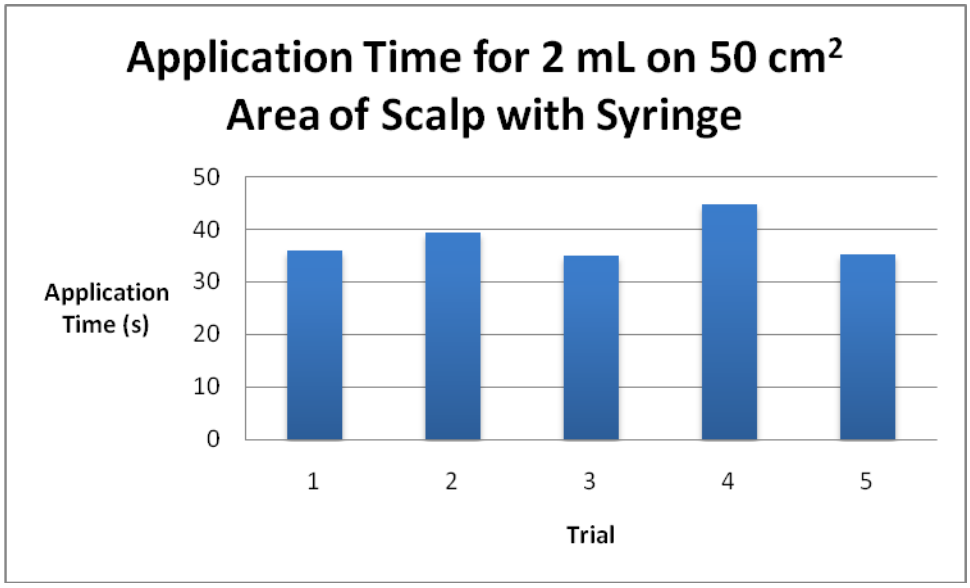

Figure 22: Graph showing application time for the drug application kit with a syringe.

Finally, the fluid distribution of the comb was tested. This was done by inserting four micro-centrifuge tubes into a strip of Play-Doh to keep them in place, and after drawing fluid into the syringe and attaching the comb, every other comb tip was placed loosely in one of the micro-centrifuge tubes (figure 23). The intention was to measure how much liquid came out of each of the tips once fluid was dispensed using the increments on the sides of the micro-centrifuge tubes. However, we observed that fluid flow was significantly uneven, and no quantitative measurements were taken. Small pieces of 0.794 mm (3/32 in) inner diameter tubing were attached to the comb teeth to lengthen the channels. This seemed to improve the evenness of flow a bit, but flow was still uneven.

Figure 23: Setup for flow distribution using syringe.

We presented our prototype and test results to our client in a meeting with the intention of determining the future of our project. He encouraged us to use the MADomizer as an applicator handle instead of the syringe with the belief that fluid distribution through the comb teeth would be more even. He also thought that a kit containing a MADomizer would be more marketable than one containing a syringe because the liquid would be dispensed from glass as opposed to plastic. We decided to pursue this suggestion, and modifications were made to the comb attachment, making the attachment diameter smaller to fit onto the MADomizer tip. The Luer-Lok tip was kept just in case the client later decides that the syringe is a better option. A rapid prototype of this final design was fabricated.

We also did a fluid distribution test with the new comb design. Three trials were done with the MADomizer spray bottle, and one trial was done with the syringe for comparison. This was done by fitting four micro-centrifuge tubes onto every other comb tip (figure 24). The comb tips were numbered 1-8 with 1 and 8 being the outermost comb tips. The device was held so that the comb tips were facing down. Once water began to come out of the comb tips after the dispenser tubes of the MADomizer were filled, twenty-eight sprays were counted out. The amount of liquid that was dispensed from each comb tip in these twenty-eight sprays was measured using the increments on the side of the micro-centrifuge tubes. The percent of water dispensed from each tip was calculated. This process was then repeated for the other four comb tips. For comparison purposes, this test was done with the syringe by putting about 1 mL of water in the syringe and attaching the comb. The micro-centrifuge tubes were attached to every other comb tip in a similar fashion, and the device was held so that the comb tips were facing down. Water was dispensed until it seemed like a micro-centrifuge tube was almost full, and the percent of water dispensed from each tip was calculated. This was repeated for the other four comb tips. As can be seen in figure 25, fluid distribution among each of the comb tips themselves was not

exactly even when using the MADomizer; however, there was consistency in fluid distribution with each individual comb tip among the three trials. It appears that there is more resistance to flow in the inner comb tip channels, observed in the general trend of the graph because less fluid was dispensed from these channels. With the syringe, fluid distribution was significantly uneven when compared with the MADomizer with fluid not even being dispensed from some of the channels. Therefore, the MADomizer is much better than the syringe with respect to evenness of fluid distribution. Additionally, qualitative analysis showed that slowly pulsing the syringe plunger resulted in a more even flow. It is therefore logical that the pulsing behavior of the spray bottle would result in a more even flow.

Figure 24: Fluid distribution testing was conducted using a rapid prototype of the comb tip attached to the MADomizer spray applicator.

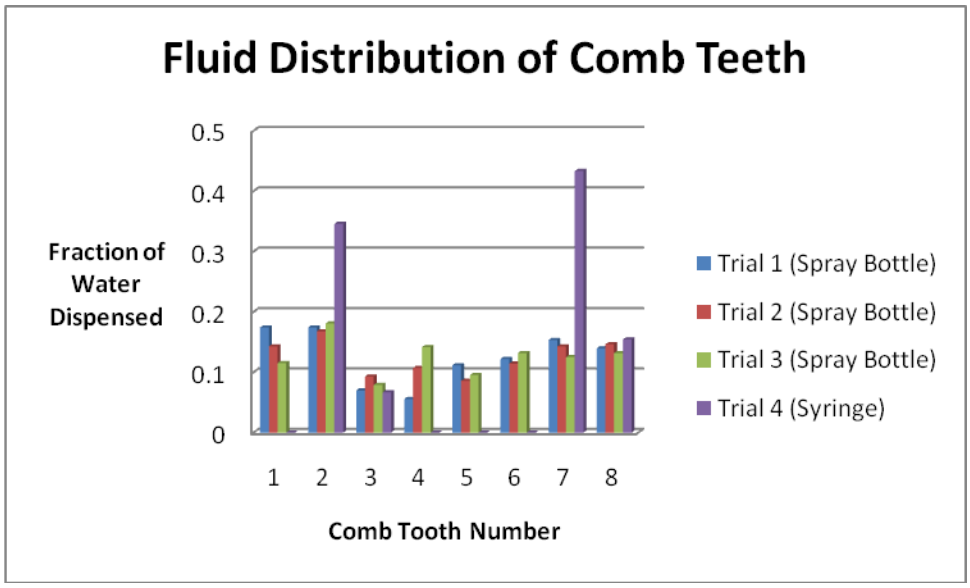

Figure 25: Graph comparing flow distribution of the comb teeth using the syringe and the MADomizer spray applicator.

The amount of dead space was also calculated for the final comb tip design with the MADomizer. Eleven trials were done by putting 2 mL of water into the MADomizer and spraying until no more fluid came out of the comb tip. The amount of liquid dispensed into the cup was measured by drawing the liquid up with the syringe. This number was then subtracted from 2 mL to determine the amount of dead space. The average amount of dead space was 0.682 mL, which is greater than the amount of dead space when using the syringe. As can be seen in figure 26, the amount of dead space for each trial with the MADomizer was greater than with the syringe; however, in each trial the amount of dead space was still less than 1 mL as our client requested.

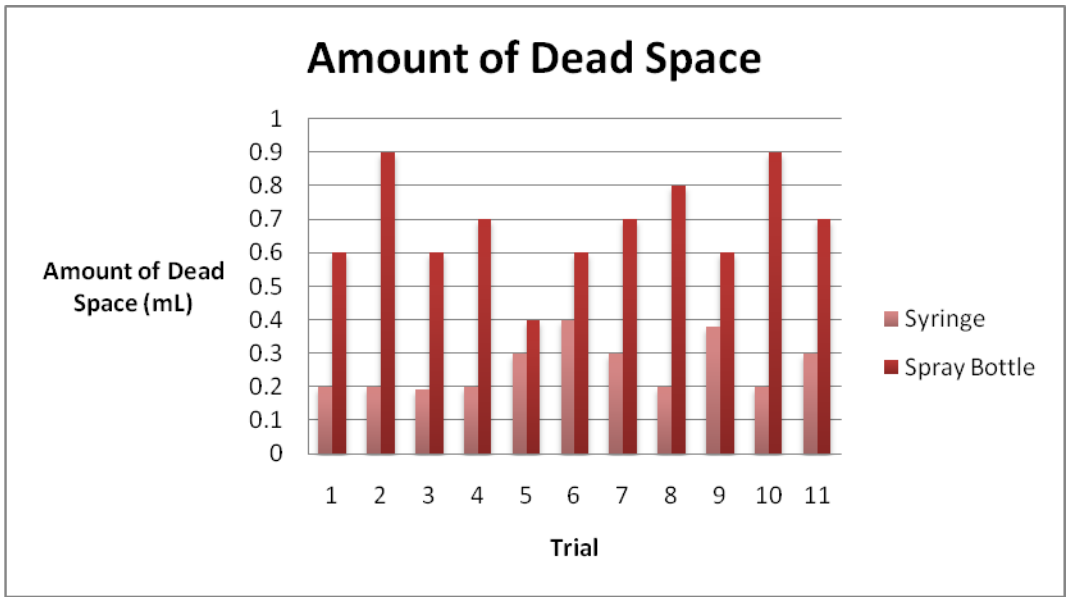

Figure 26: Graph showing dead space of the syringe vs. the spray bottle.

An application time test was not completed with the MADomizer because the connection between the comb and the spray bottle was not ideal, and combing through hair would cause the comb to fall off.

Due to these test results, we concluded that the MADomizer with the compatible comb tip is the best design; however, there is a tradeoff between dead space and fluid distribution. Even though there is more dead space in the MADomizer than in the syringe, the amount of dead space is still less than 1 mL, as our client desired. It is worth using the MADomizer instead of the syringe due to the significantly greater evenness of fluid distribution. When it comes to applying the drug solution, evenness of distribution is more important than amount of dead space. While time trials were not conducted with the MADomizer, we do not anticipate that the application process will take too long because the client currently uses the MADomizer to apply the drug solution to test subjects' scalps, and he has no complaints. However, if our client does decide later that the syringe is better than the MADomizer for applying solution, he still has the option to use the syringe because the Luer-Lok connection is still incorporated in the final comb tip design.

Cost

Table 4: Cost of direct digital manufacturing and injection molding fabrication methods.

Fabrication Method	Company	Cost	The Product
Direct Digital Manufacturing [10]	RedEye	$30	Price for a single comb tip
		$21	Price per unit if purchased in bulk
Injection Molding [12]	Engineering Industries, Inc.	$20,000	Price for a two-cavity family injection mold of comb tip design

As shown in table 4, the cost of injection molding is significantly higher than the cost of direct digital manufacturing. Direct digital manufacturing would be economical if only a few parts were needed. Injection molding would be economical if thousands of parts were needed because the mold would end up paying for itself. At this time, both of these fabrication methods are unsuitable and uneconomical for our client at this time. He needs 600-700 comb tips to use for clinical testing of his company's drug. The comb component of the current device that he uses for application of the drug solution is a hair dye comb from a L'Oreal hair dye kit. To get this comb he must purchase the whole hair dye kit, which costs $12. This cost is less than both fabrication methods shown above. However, if our client wanted to include our comb with his drug solution once it is FDA approved, it might be economical for him to get an injection mold made of the comb tip because he would require a greater number of comb tips than he does now and the mold would end up paying for itself. All of this is up to the discretion of the client, of course, and we are merely giving him information and suggestions.

Ergonomics

It is important that the comb applicator does not cause any discomfort for the patient or the CRA administering the drug solution. The final kit for the device will be equipped to manage both types of comfort.

As mentioned in the comb tip design alternatives sections, there are two main ways to make the comb tip more comfortable on the patients scalp. First, gradually shortening the comb's inner teeth would create a contoured shape as shown in figure 27. The contoured shape should not add any additional difficulty to the design and fabrication of the linear branched tip. It is also possible to make the comb contoured by designing the comb flexed which will also create a contour better shaped for the human scalp. Another option for patient comfort is to add flexibility to the comb's teeth by choosing a more pliable plastic for the comb. The chosen plastic must balance flexibility for comfort on the scalp and sturdiness for combing through the hair.

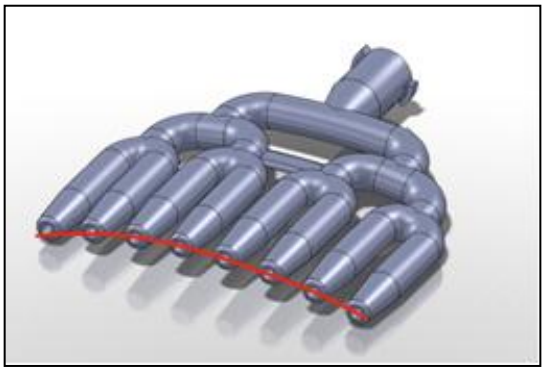

Figure 27: This linear branched tip has contoured comb teeth (as shown by the red line) to prevent patient discomfort.

The advantage of the MADomizer is in the control it gives the CRA but is rather cumbersome and tiring to use. After applying approximately 20 sprays per patient, there is a potential for pain and discomfort in the CRA's hand. To cope with this possibility, it is advantageous that the spray bottle is ambidextrous. The user can switch between hands throughout the day, as well as between both the thumb and index finger on each hand. The use of four different fingers drastically decreases the potential discomfort for the user and ensures that the device does not cause excess hand cramping.

Ethical Considerations

The primary ethical concern for this project is patient safety throughout the trials. This means that the comb tip should be comfortable for a patient with sensitive, irradiated skin, even after repeated use. Also, our device must avoid natural latex due to potential patient allergies. The device should be disposable to prevent any cross-contamination that could occur with multiple uses. Lastly, the device should comply with IRB safety standards.

Future Work

Although much effort was spent to create a final design that is completely ready for use in clinical trials, there remains some future work to be done before the device is ready to be used for clinical trials. First, the final design should once again be tested using the MADomizer. During our last testing session, the comb tip was designed to the exact specifications of the MADomizer tip using SolidWorks; however, the rapid prototyping machine did not print with adequate accuracy and, as a result, the comb tip did not fit well onto the MADomizer. The SolidWorks design should be accurate, so this problem is only a matter of testing that the fabrication process can be accurate enough to form a secure attachment.

Additional testing could also be performed using the final design to apply solution to the scalp. In our testing, we conducted on scalp testing using the syringe and just one test subject. In the future, it may be a good idea to continue on scalp testing using the MADomizer, as we have chosen for our final design, to ensure that it can accurately, comfortably, and efficiently apply solutions to the desired area of scalp. In the future, if our client decides to switch the design to use the syringe instead of the MADomizer, we have left the option open by keeping the Luer-Lok attachments on the comb tip.

Finally, the device must be manufactured to obtain several hundred copies. Although we researched a number of options as outlined in the recommendations to client section, we certainly have not exhausted the manufacturing possibilities and we leave the final decision for manufacturing up to our client.

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Appendix

Product Design Specifications: Topical Pharmaceutical Application Device for Scalp

Topical Pharmaceutical Application Device for Scalp

September 15, 2010

Vanessa Grosskopf, Rachel O'Connell, Samantha Paulsen, Jeff Theisen

Problem Statement:

Human cancer patients receiving a 30-day course of radiotherapy for head and neck cancer must have solvent containing drug applied topically to their scalps to prevent alopecia. This is done using a hollow comb applicator that applies a specific amount of solvent to a specific area of the scalp. The client desires a device that will accurately dispense the drug and have a professional appearance so that it complies with the Institutional Review Board (IRB) standards for use in clinical trials.

Client Requirements:

- Applicator must deliver drug solution to the scalp while minimizing amount wasted on the hair
- Deliver 2.0 mL ± 5% to a 50 cm^2 area of scalp
- One-time use and completely disposable
- Limit the amount of dead space to 1.0 mL to minimize costs associated with wasted drug
- Application process must be quick and clean

Design Restraints:

1. **Physical and Operational Requirements**
    a. *Performance requirements:* The device should be designed for single use in a clinical trial setting to deliver 30% water/70% ethanol solution with drug directly to a patient's scalp. The application process should be comfortable and take between 60-90 s. The device should limit the amount of dead space to 1.0 mL.
    b. *Safety:* The applicator must pass the standards of the Institutional Review Board (IRB).
    c. *Accuracy and Reliability:* The applicator should uniformly deliver 2.0 mL ± 5% to a 50 cm^2 area of scalp and minimize dripping of the solution.
    d. *Life in Service:* The device will be disposable for one-time use.
    e. *Shelf life:* Since the clinical trials will take approximately 1-2 months, the device should last at least 3-6 months.
    f. *Operating Environment:* The device will be used in a clinical study by a clinical research assistant.
    g. *Ergonomics:* The device should be comfortable for a nurse to hold and use. The comb attachment should not cause any discomfort when used repeatedly on the scalps of patients with sensitive, irradiated skin. A flexible comb with a slightly

curved shape arrangement of tips would follow the contours of the scalp better than a rigid comb and would therefore be more comfortable for the patient.

h. *Size:* The device should be hand-held.
i. *Weight:* The device weight should be less than 0.5 kg.
j. *Materials:* The materials used in the device should be compatible with a 70% ethanol solution containing drug. Natural latex should not be used due to potential patient allergies. The client suggests that glass, stainless steel, or plastic is used.
k. *Aesthetics, Appearance, and Finish:* The device should look professional enough to be accepted by the IRB and FDA for clinical trials.

2. Product Characteristics

a. *Quantity:* The client requires one device as a proof of concept. Ideally, 300-400 would be required for clinical trials.
b. *Target Product Cost:* $200-400, could be increased with client approval

3. Miscellaneous

a. *Standards and Specifications:* The applicator must pass the standards of the Institutional Review Board (IRB).
b. *Customer:* The device will be used in a clinical trial at the UW Hospital.
c. *Patient concerns:* Other than general safety concerns, there are no special considerations for the device since it is one-time use.
d. *Competition:* Due to the fact that the device is custom to this specific research lab, there is no foreseen competition; however, there is the potential to integrate current hair dye applicator combs into our design.

Testing Data

Table 5: Flow distribution data derived from field testing. The spray applicator took 28 sprays to dispense liquid.

	Trial 1 (Spray Bottle)	Trial 2 (Spray Bottle)	Trial 3 (Spray Bottle)	Trial 4 (Syringe)	AVERAGE (Spray Bottle)	Standard Deviation (spray bottle)
1	0.174216028	0.142857143	0.115131579	0	0.14406825	0.029561
2	0.174216028	0.167857143	0.180921053	0.345744681	0.174331408	0.006533
3	0.069686411	0.092857143	0.078947368	0.066666667	0.080496974	0.011663
4	0.055749129	0.107142857	0.141447368	0	0.101446451	0.043132
5	0.111498258	0.085714286	0.095394737	0	0.09753576	0.013025
6	0.12195122	0.114285714	0.131578947	0	0.122605294	0.008665
7	0.153310105	0.142857143	0.125	0.433333333	0.140389082	0.014316
8	0.139372822	0.146428571	0.131578947	0.154255319	0.13912678	0.007428
Total	1	1	1	1		

Table 6: Dead Space data for syringe and MADomizer spray applicator

Dead Space (Syringe)												
1	2	3	4	5	6	7	8	9	10	11	**Average**	**Standard Deviation**
0.2	0.2	0.19	0.2	0.3	0.4	0.3	0.2	0.38	0.2	0.3	0.260909	0.078544
Dead Space (Spray Bottle)												
1	2	3	4	5	6	7	8	9	10	11	**Average**	**Standard Deviation**
0.6	0.9	0.6	0.7	0.4	0.6	0.7	0.8	0.6	0.9	0.7	0.681818	0.147093

Table 7: Application time data for syringe.

Application Time (2 mL on 50 cm2)						
1	2	3	4	5	**Average**	**Standard Deviation**
36	39	35	45	35	38.002	4.077366797

Cost of Materials

Table 8: Cost of the materials purchased to build a branched comb for preliminary testing.

Item/Material	Cost
10 feet of 1/32'' inner diameter tubing	$5.78
10 feet of 3/32'' inner diameter tubing	$9.47
10 Y-connectors for 3/32'' tubing	$6.76
Pliobond	$8.40
	Total: $30.41