# Topical Pharmaceutical Application Device for Scalp

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## Abstract

One of the most noticeable side effects of radiation and chemotherapy for cancer patients is alopecia, or hair loss. Both chemotherapy drugs and radiation reduce tumor size by targeting and destroying rapidly dividing cells, including stem cells within hair follicles. The pharmaceutical company Procertus has developed a drug called 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 drug to a patient's scalp. The device currently used by the company consists of a L'Oreal hair dye comb attached to a Wolfe Tory Medical MADomizer spray applicator. The two components are connected using a simple rubber stopper. However, the current device may not pass standards set by the Institutional Review Board (IRB) because it appears unprofessional, the rubber elements could cause allergic reactions, and each applicator is excessively 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 9) compatible with the threaded Luer-Lok tip of a syringe, a 5 mL syringe, 2 mL worth of drug dissolved in a 70% ethanol solution, and a syringe handle. This new design appears professional, accurately and evenly dispenses the drug solution, can apply the drug quickly, and is comfortable for both the certified research assistant (CRA) applying the drug and patient. To further this project, our group must fabricate the comb tip, purchase other elements of the kit, and test the performance of the final device to ensure it can pass IRB standards.

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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 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].

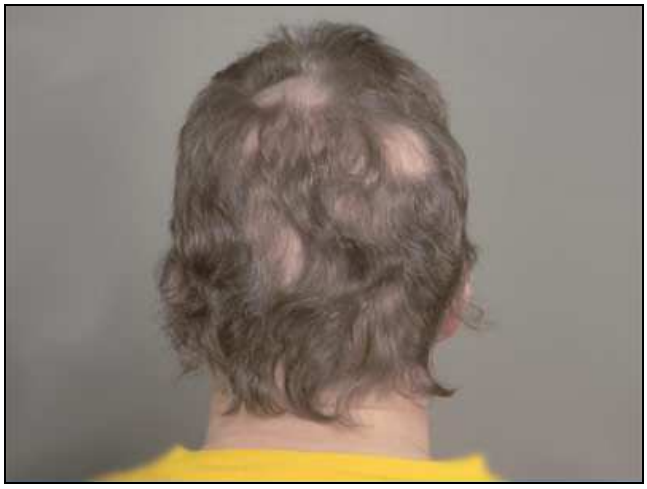

**Figure 1: Image of hair loss due to chemotherapy [4].**

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.

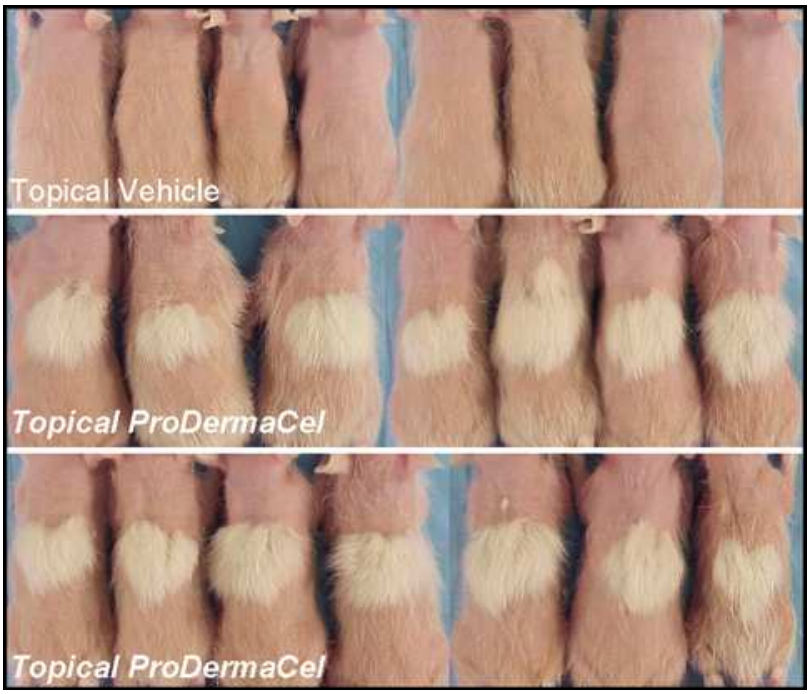


**Figure 2: Images of initial testing using ProDermaCel in mouse models receiving radiation therapy. The drug effectively prevented hair loss in early trials [3].**

## 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 second 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

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 a small glass vial, or ampoule, 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.

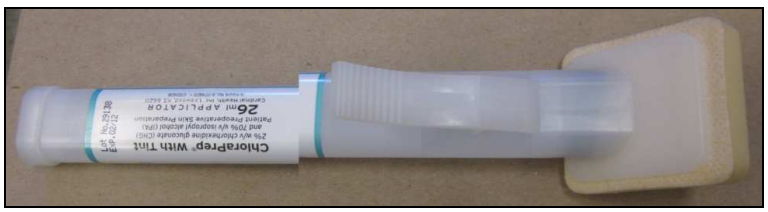


Figure 6: ChloraPrep Frepp Applicator, containing drug solution within a small glass vial that can be broken using the side arm to dispense the drug solution.

## 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.

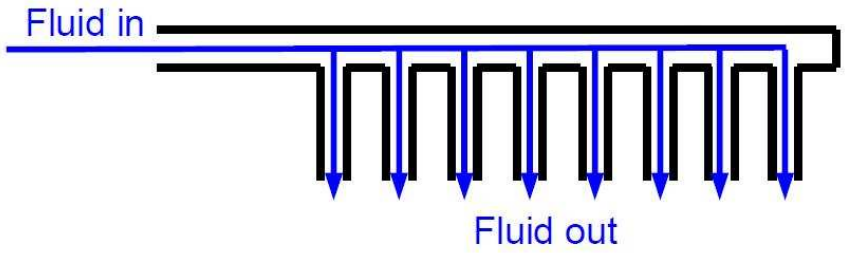


Figure 7: The straight comb tip, with the flow of the drug solution shown in blue.

### 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.

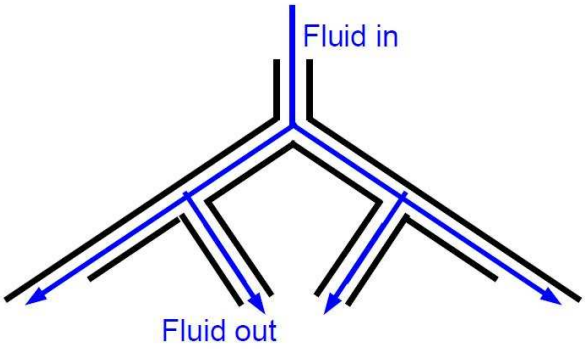


Figure 8: The angled branch comb, with the flow of the drug solution shown in blue.

### 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 ninety degree 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 3. 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.

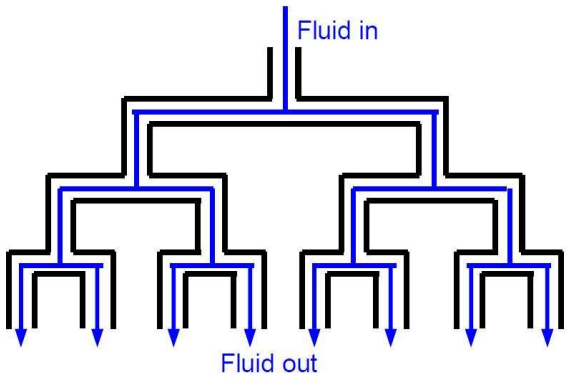


Figure 9: The linear branched tip, with flow of the drug solution shown in blue.

## 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 ninety degree angles. The ninety degrees 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 one inch, 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 ninety degree 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.

## Testing

To get a better 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 2.381 mm (3/32 in) and 0.794 mm (1/32 in) inner diameters], white nylon Y-connectors [2.381 mm (3/32 in) inner diameter], and rubber cement. A table of the cost of these materials can be found in the appendix in table 3. These materials were assembled to create a branching comb that began as one channel and branched into eight, as shown in figure 12.

**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 13. 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 14. 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.

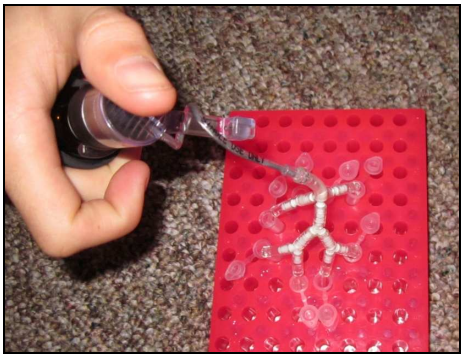

**Figure 11: Shows the setup of the collection tubes used to test the evenness of fluid flow in the preliminary comb designs.**

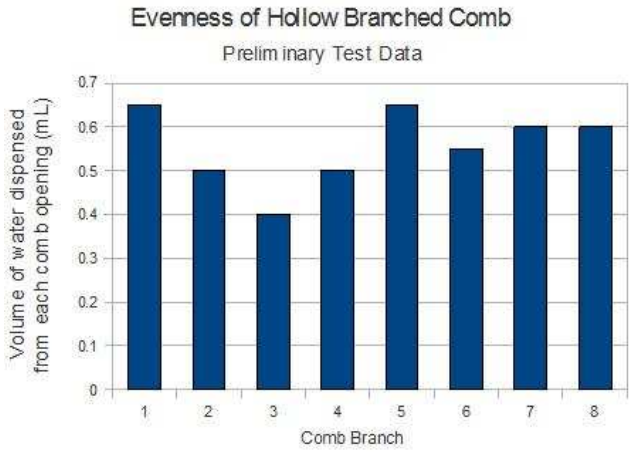


**Figure 12: Data from evenness test shows that the flow from the prototype comb was generally even, but not perfect. With a professionally fabricated comb, it is expected that the distribution more equal because the fluid resistances in each branch will be closer to equal.**

## Final Design

Based on our design matrices and our preliminary testing results, the two components chosen for our final design are the linear branched comb and the syringe reservoir. Our final design consists of a kit that includes a syringe, a linear branched comb, a solution vial, and a handle for the syringe (figure 10). The syringe will have the male Luer-Lok taper at the tip and will be purchased by the team. The size of the syringe purchased depends on the amount of solution that needs to be dispensed, but for our purposes we will purchase a 5 mL syringe. The comb will be fabricated to have the female Luer-Lok taper so that it could be easily screwed on to the tip of the syringe. The number of branches in the comb must be finalized. The material for the comb also has to be researched and determined. The material will be chosen based on a combination of how well it will be able to comb through hair and how comfortable it will be for the patient. The comb will be contoured to better fit the shape of the human head to enhance patient comfort. A vial for solution will be purchased from a source that has not yet been determined. The only consideration for this is that it should be easy to draw all of the liquid out of it with the syringe. We are also considering purchasing a syringe handle which would enhance comfort for the CRA. Some preliminary research has been done to determine potential vendors of syringe handles, but nothing has been finalized as to which handle we will purchase.

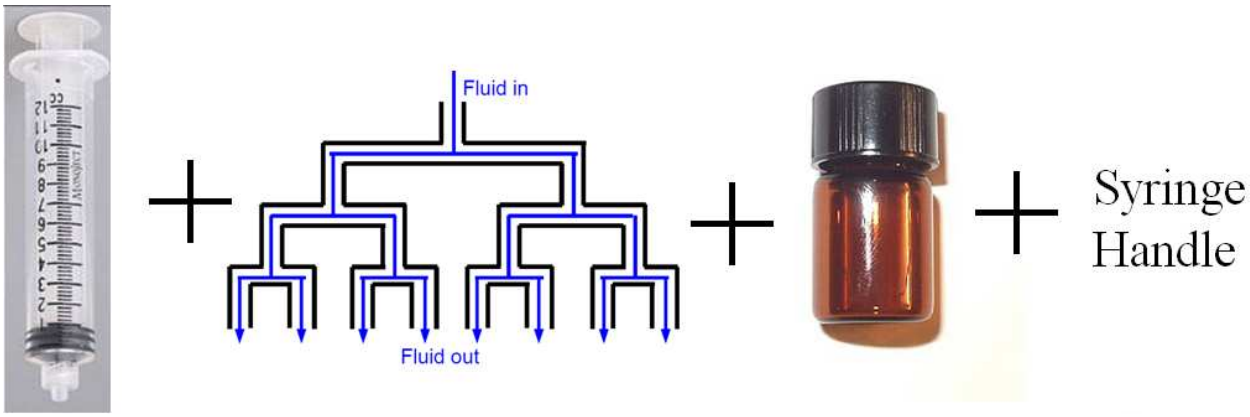


**Figure 13: Contents for the final drug delivery kit include a 5 mL syringe with a Luer-Lok tip, a linear branched hollow comb tip, a vial containing the drug solution, and an ergonomic handle for the syringe [7] [5].**

## 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 11. The contoured shape should not add any additional difficulty to the design and fabrication of the linear branched tip. Another option is to add flexibility to the combs 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.

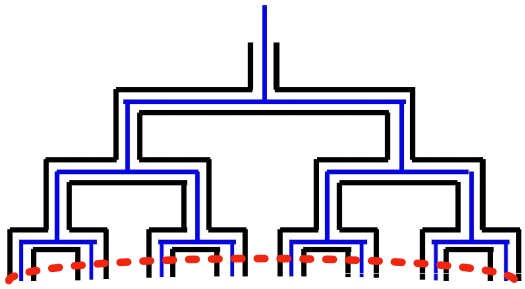

**Figure 14: This linear branched tip will have contoured comb teeth to prevent any discomfort to the patient. The contour is shown by the red dotted line.**

Syringes in general can be cumbersome for some people to hold and control. In order to give the CRA proper comfort and control of a device they use several times a day, a syringe handle will be included in the kit. The exact handle has not been decided upon yet, however there are several handles commercially available to choose from. All of the options will give the CRA a larger holding area and allow the CRA to depress the syringe plunger by squeezing a handle or using a trigger-like finger hold. The syringe handle will ensure that the CRA will be comfortable during the process and should help eliminate 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

Looking forward to the rest of the semester, most of the effort will be committed to fabricating and testing the final product. Fabrication will include creating a SolidWorks ® file of the branched comb, deciding on a material, getting a quote from a plastic manufacturing company, and obtaining a manufactured part. Additional parts will be purchased to complete the application kit, including a syringe, a vial for storage, and potentially a handle for the syringe to make it more ergonomic. Testing will include evaluation of the final design's accuracy, speed, and evenness of application. Fabrication and testing are elaborated on in the following sections.

## Fabrication Process

The final design kit consists of a syringe, a vial for storage of drug, a hollow comb, and potentially a handle for the syringe. Of these items, only the hollow comb tip will need to be fabricated, while the rest can be purchased. The end of the comb that interfaces with the syringe must be designed to adhere to the Luer-Lok specifications, illustrated in figure 15. The rest of the tip could follow any design desired to best fit the purpose of delivering drug to the scalp; ideally, it would contour to fit the curvature of the scalp by means of using a flexible plastic or by designing the comb to have a curved-cut that fits the scalp.

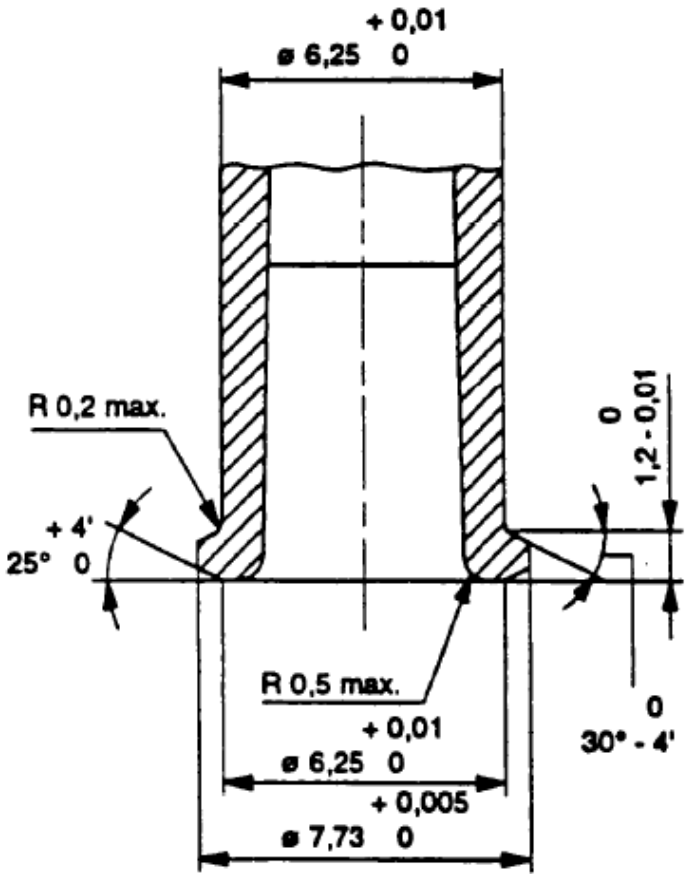


Figure 15: Schematics for a female Luer-Lok system with dimensions in mm [8].

To attain the highest quality comb, the device would be fabricated by a professional plastics manufacturing company/facility. One possibility is to utilize the services of Proto Labs, which include rapid CNC machining or injection molding of parts. To get a part fabricated by Proto Labs, the team would have to create a SolidWorks® file of the part. Once the SolidWorks® file has been created, it can be uploaded to the Proto Labs website and they will return a quote for the fabrication. Based on the example quotes, this process may be hundreds of dollars, so this option will be discussed with the client once a SolidWorks® design has been created. If this plan falls through, there are a number of options to pursue: we could discuss other facilities to get a prototype fabricated with members of the Polymer Research Center on campus or we could potentially use the rapid prototyping machine that will soon arrive in the BME department.

Another factor to consider for fabrication is the material to use. The comb should be rigid enough to part through the hair and reach the scalp, but it should also be soft and flexible enough to contour to the curvature of the scalp and be comfortable for patients. The team plans to discuss this issue with members of the Polymer Research Center. We have already attempted to contact two different members though email; however, we have received no response yet. Therefore, we plan to visit their offices on campus to see if they are willing to give us advice on plastic materials. Alternatively, the Proto Labs website offers a table to guide users on material selection, which contains information such as strength, dimensional accuracy, cost, and more. This table is shown in the appendix in table 4.

## Testing

There are a number of tests that will be performed on the final device, including tests of accuracy, evenness, and speed of application. Since the device must deliver 2.0 mL ± 5% to a 50 $cm^2$ area of scalp, it needs to be tested to ensure that it is within this range. This will be accomplished by collecting the amount of liquid delivered for a number of trials and checking that it meets the requirements. Evenness will be evaluated by coloring the liquid using a food dye, applying it to a surface using the device, and assessing the distribution of color. This will be tested both on a flat surface such as paper, as well as on scalp. If the device distributes the drug solution evenly, the entire surface should appear to have the same amount of color, with no portion receiving more dye than the others. This test will also assess the cleanliness of application, as drips will be easily visible with the food dye. Speed must be evaluated because the final application process should be less than 90 seconds, in order to reduce the amount of time required to prepare patients for radiation therapy. This will be tested by simply timing the length of the application process, ensuring that the application does not become sloppy if rushed.

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# Appendix

## Product Design Specifications: Topical Pharmaceutical Application Device for Scalp

### Topical Pharmaceutical Application Device for Scalp

September 15, 2010

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**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 seconds. 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. Material Properties

## Cost of Materials

Table 3: Table of the 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** |

## Material Properties

**Table 4: Table of material characteristics from Proto Labs, used to assess plastic properties for the comp tip [9].**

| | | Mechanical Properties | | | Moldability Characteristics | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Resin Generic Name | Some brand names | Strength | Impact Resistance | High Temp. Strength | Warp and Dimen-sional Accuracy, Molded | Fills Small features | Voids in thick sections | Sink in Thick Sections | Flash | High Temp. hard on Mold & Ejectors | Relative Cost |
| Acetal | Delrin, Celcon | Medium | Medium | Medium-Low | Fair | Fair | Poor | Good | Good | Fair | Medium |
| Nylon 6/6 | Zytel | Medium | High | Low | Fair | Excellent | Good | Fair | Poor | Fair | Medium |
| Nylon 6/6, glass filled | Zytel | High | Medium | High | Poor | Good | Excellent | Good | Fair | Fair | Medium |
| Polypropylene | Maxxam, Profax | Low | High | Low | Fair | Excellent | Poor | Poor | Poor | Good | Low |
| High Density Polyethylene (HDPE) | Dow HDPE, Chevron HDPE | Low | High | Low | Fair | Excellent | Unknown | Poor | Poor | Good | Low |
| Polycarbonate | Lexan, Makrolon | Medium | High | Medium High | Good | Fair | Fair to Good | Fair | Good | Good | Medium High |
| Acrylonitrile Butadiene Styrene (ABS) | Lustran, Cycolac | Medium-Low | High | Low | Good | Fair | Good | Fair | Good | Good | Low |
| Polycarbonate / ABS Alloy | Cycoloy, Bayblend | Medium | High | Medium | Good-Excellent | Fair | Good | Fair | Good | Good | Medium |
| Polybutylene Terephthalate | Valox, Crastin | Medium | High | Low | Fair | Fair | Unknown | Fair | Fair | Good | Medium High |
| Polybutylene and Polyethylene Terephthalate, glass filled | Valox, Crastin, Rynite | High | Medium | Medium | Poor | Fair | Good | Good | Fair | Fair | Medium High |
| Polystyrene | Styron | Medium-Low | Low | Low | Good | Good | Unknown | Fair | Fair | Good | Low |
| Thermoplastic Elastomer | Isoplast, Santoprene | Low | High | Low | Poor | Excellent | Excellent | Good | Poor | Excellent | Medium-Low |
| Acrylic | Plexiglass, Acrylite | Medium | Low | Low | Good | Fair | Excellent | Good | Good | Good | Medium |