ARTICLE

Multiple Sclerosis Image-Guided Subcutaneous Injections Using Augmented Reality Guided Imagery

Donya Meshgin and Marta Kersten-Oertel
Gina Cody School of Engineering and Computer Science, and PERFORM Centre, Concordia University, Montreal, Canada

ARTICLE HISTORY
Compiled September 6, 2020

ABSTRACT
In this paper, we explore how new technologies can be used to improve Multiple Sclerosis (MS) treatments. Treatment of MS most often includes self-injecting medicine into the subcutis, the tissue layer between the skin and the muscle. The injections can make a patient’s skin sore, red, itchy, and even cause pain, thus many patients suffer from injection anxiety. The aim of our work is to determine whether an application based on augmented reality (AR) technology can help reduce patients’ injection anxiety and perceived pain during the administration of their medication. An AR application, MSease, that allows MS patients to visualise injection sites with the help of an overlaid AR grid which also serves to keep track of their previous injections, was developed. An MS patient and people without MS were consulted in order to assess the quality of the application. The results of this research indicate a marked reduction in injection anxiety and a minor reduction in perceived pain when using our application.

KEYWORDS
Augmented reality; Multiple Sclerosis; injection anxiety; perceived pain; image-guidance; subcutaneous injections; mHealth

1. Introduction
People diagnosed with multiple sclerosis (MS) typically use medication that must be administered via subcutaneous injection. They must rotate between seven injection areas to avoid picking the same site within a week; this is accomplished by keeping a log of their recent injection sites. This is typically done by using an injection grid provided by their physician. However, it may be difficult to visualize the injection grid on their own body, i.e. map the injection grid from the journal to where it should be on their body. This makes it unclear as to where an appropriate injection site is. Additionally, MS patients must also keep track of their post-injection reactions and symptoms. Currently, there are a few mobile health (mHealth) apps and physical journals that are available for those affected by MS, but they are poorly rated as they do not cater to their frustrations and needs (e.g. (13) (14)). Furthermore, many MS patients experience self-injection anxiety. To overcome this, many healthcare providers suggest using an imagination-based stress management technique called guided imagery at the time of injection. However, this can be difficult to do while performing the injection itself. In this paper, we aim to provide a solution to easing an MS patient’s treatment
process by exploring whether an augmented reality (AR) mHealth application for medicine administration logging, image-guided injections and guided imagery therapy is an effective MS tool.

2. Related Work

According to Statistics Canada, the prevalence of MS among Canadians is the highest in the world, with 290 cases per 100,000 (3). For these MS patients, beginning a self-injection-based treatment is difficult to adapt to. Adjustment is the core principle of adapting to MS and adhering to a new medication. In (2), the authors described how Injection Anxiety (IA) is the primary factor of non-adherence at every time point evaluated. IA can prevent MS patients from getting through their treatment properly, or can even cause them to terminate it entirely. It is for this reason that healthcare providers suggest patients use their imagination for guided imagery to mitigate their stress and pain (8; 2). A meta-analysis of the effectiveness of complementary therapies, performed by Deng and Cassileth (1), found that such practices are effective at easing the physical and emotional toll of cancer treatments. Complementary therapies include relaxation techniques, guided imagery, and similar approaches to mindfulness-meditation. While these therapies are by no means a replacement for clinical treatment, they have been found to alleviate some of the symptoms associated with intense medical treatment. According to Schneider et al. (8), who studied the effectiveness of using virtual reality as a means of distraction during symptoms of distress during chemotherapy, these types of techniques can be effectively used in parallel with medical treatment.

We believe that using an AR application on a smartphone will reduce injection anxiety and the perceived pain during the injection process for MS patients. Specifically, using AR during MS treatments may ease patients’ self-injection journey, and improve the accuracy and comfort levels of the procedure, since mistakes such as injecting directly into the muscle instead of the subcutis regions may decrease. Furthermore, mistakes due to injecting to recently used sites should also be decreased. To this end, we have developed an mHealth app that provides a guided imagery experience and an injection grid overlay as an image-guided medicine administration tool. Image-guided AR systems for needle placement have already been shown to be an effective and accurate navigation tool in various medical areas (e.g. (10; 12)).

To understand the problem space adequately, a recently diagnosed MS patient was involved throughout every step of this project. Furthermore, we first looked at current solutions to MS injection treatments. The most common is a physical journal that the MS patient uses to keep track of their treatment dates, the corresponding area the medicine was administered in, and their post-injection symptoms (see Fig. 1). There are also a few mHealth smartphone applications that exist to simulate the traditional journals, but they either have low-rated reviews due to poor usability (difficulty navigating the application, logging into account and accessing data) or they do not contain metrics specific to injections (see Fig. 2). Smartphone applications in the context of multiple sclerosis management have been shown to provide users with a feeling of independence and ease (5). In a recent survey of 164 iOS and Google Play applications for people diagnosed with MS, only 10 apps were designed for medication self-management (7). Among those applications, the majority focused on injection tracking and management (recording medication name, dosage, and administration sites), medication reminders (medication stock renewals, time of injection), and note
recording to name a few. However, none of the applications provided an augmented reality visualization to aid MS patients with stress-relief or image guidance for injections specifically during their medication administration. Giunti et al. (4) further showed that some of the barriers to the adoption of mHealth apps for Multiple Sclerosis are usability-based, more precisely unattractive design, confusing interface, and issues pertaining to accessibility. As such, an important focus in our work was on user interface (UI) design, and not just on AR image guidance and guided imagery.

(a) Example of an injection journal for keeping track of injection days and times. (b) Example of paper injection journal for site location.

Figure 1.: Currently, most often a paper-based journal (by COPAXONE®) is used to keep track of (a) when injections were done and (b) at which location.

3. System Design

We designed an AR application, MSease, composed of the four following features: an AR injection grid overlay for each possible medicine administration site, an AR mascot for visual guided imagery, a journal that logs injection information, and reminders for injection times. The application was developed with Unity for Android and was written using C#, using Unity’s AR Foundation framework and the Vuforia Augmented Reality SDK. The main features of the application are covered in more detail below.

3.1. Injection Site Overlay Grid

Using AR, an injection grid is overlaid on the user’s body part (abdomen, thigh, arm, buttock) and currently available injection sites are determined using data from the previous injections which are stored in the journal (see Fig. 3). The shape of each injection area, that is the grid of injection sites for each body part, was determined from the patient’s injection paper journal by COPAXONE® (Glatiramer Acetate Injection)(see Fig. 1 (b)). The injection overlay appears upon detection of an AR marker,
an image target that we have set as a QR code with the MSease logo in the center using the Vuforia Target Manager database for the project. To ensure the accuracy and consistency of the placement of the grid on the user’s body, the injection grid placement is determined upon onboarding (i.e. initial in-app guidance that highlights key benefits and features of an app). The user prints the given QR-code target on adhesive paper and places it onto the body part in the correct spot, as specified on the onboarding. The injection grid is color-coded to indicate the possibility of using a specific injection site; places that are available for injection are displayed as light blue squares. The most recently injected sites are pink, and a blue-to-pink gradient scale indicates how recently a given injection site was used (see Fig. 3 (a)). In order to begin an injection at a particular area, the user must tap on one of the seven options shown in Fig. 3(a). This allows for the correct overlay grid to be dynamically generated upon target detection. For each of the seven possible injection areas, the user will place the same target sticker at the appropriate area. Once the user wishes to begin the injection, they can tap their finger on the exact injection site. This highlights a square on the grid overlay (see Fig. 4 (b)), where the user is prompted to place a finger from their free hand on their body part within that square. The selected square’s ID will get sent to the Journal module in order to keep track of all injections. Then the user may put their smartphone down and commence the injection.
3.2. 3D Mascot

The mascot is aimed at providing the user with pain therapy and relief from injection anxiety during the medication administration process. As described above, guided imagery has been found to be helpful in calming the patient during difficult or trying treatments. However, the stress associated with the injection process may make a patient unable to imagine a calming place, person, or idea. The visual nature of the 3D mascot will remove the extra step of imagining another situation; it diverts the attention of the patient in order to relieve their stress and facilitate them into a more relaxed mindset. An appropriate candidate for a mascot is a 3D model that is animated, since the animate motion of objects grasps the visual attention of a person (6).

The 3D model itself is an AR rendering of an avatar chosen by the user. Possible examples include cute animals like cats or dogs, and popular anime characters to name a few. Giving the user a choice between a variety of mascots ensures the feature’s effectiveness as it will give the user a more personalized experience. The mascots are 3D models provided by the SketchFab plugin for Unity, while Vuforia and Unity’s AR foundation solution is used to display the mascot on AR-compatible smartphones; the one we have chosen as default is an animated robot that waves and smiles while playing with its toolbox (15).

The mascot is displayed in the same scene as the injection grid, as it is where the user is most in need of support. This feature is optional and is configurable within the
settings of the application.

Figure 4.: A view of the AR Overlay grid and 3D Mascot (a) when the user first opens it the first time (b) when the user selects an injection site (c) when the user has logged previous injections for that area.

3.3. Journal

The journal is implemented as a standard mobile application feature and used to log information related to the injections such as the date and time of an injection, the selected injection site and the necessary needle depth to administer the medication in that specific area. The journal will also allow the user to record how they felt during an injection by rating their experience on an ordinal scale from 1 to 10. Additionally, each journal entry includes a checkbox to confirm that the user has cleaned the injector as well as the selected site grid associated with the injection for that day. During the time of injection, the user will be able to select the grid of one of seven possible subcutaneous injection sites in order to launch an injection activity with Unity.

4. Evaluation

In order to determine if MSease reduces injection anxiety and the perceived pain during the injection, we received feedback from one MS patient using the app. Unfortunately, due to the onset of the COVID-19 pandemic and cancelling of all human subject studies at our institution, a larger study was not possible. Furthermore, due to the many usability and interface design barriers found with the majority of MS apps (4; 5), we had 14 participants (without MS) test the application in terms of ease of use. As the main features of MSease, i.e. augmented reality injection site visualization and guided imagery for reducing anxiety and pain, are not available (to the best of our
knowledge) in any other MS medication self-management app, we were not able to directly compare to other MS applications.

4.1. MS Patient Study

Our only participant with MS was a 23-year-old female with injection anxiety. She was asked to describe the difficulty she experienced in performing her injections for two weeks prior to using our system. She then used our system and recorded the same data over a similar two-week period. After the completion of the testing phase, we aggregated the data over the two-week periods and compare them to determine if our participant experienced an improvement. Throughout the development of the project, unstructured interviews took place periodically with the participant in order to gain iterative criticism of the system. Additionally, we asked the participant to complete a survey describing their experience using MSease and how well they thought it helped to alleviate their anxiety and pain.

4.2. MSease App Usability Evaluation

Due to the limited number of available participants with MS, our population sample included 14 users without MS, which were used to mainly evaluate the user interface and workflow aspects of our application not directly related to the reduction of injection anxiety and perceived pain such as the positioning of the AR grid as well as the general usability criterion of our application.

The study began with a pre-test questionnaire (see Table 1). After the pre-test questionnaire, all participants were asked to interact with MSease following the instructions below which allowed them to explore the app and guided them throughout the study.

<table>
<thead>
<tr>
<th>Question</th>
<th>Reasoning</th>
</tr>
</thead>
<tbody>
<tr>
<td>How familiar are you with Mobile Applications?</td>
<td>To evaluate the user’s prior experience with mobile applications.</td>
</tr>
<tr>
<td>How familiar are you with Augmented Reality?</td>
<td>To evaluate the user’s prior experience with augmented reality applications.</td>
</tr>
<tr>
<td>How many times a week do you do your injections?</td>
<td>To evaluate how frequently the user is required to take their medication.</td>
</tr>
<tr>
<td>How do you cope with injection anxiety?</td>
<td>To evaluate the user’s current method of dealing with injection anxiety.</td>
</tr>
<tr>
<td>Do you experience injection anxiety?</td>
<td>To evaluate if the user experiences injection anxiety.</td>
</tr>
<tr>
<td>How useful do you think journals are for tracking injection areas?</td>
<td>To evaluate the user’s view on journals in terms of usefulness for tracking injection areas.</td>
</tr>
<tr>
<td>How would you describe your perceived pain during injection?</td>
<td>To evaluate the severity of pain experienced by the patient.</td>
</tr>
<tr>
<td>What is one thing you would change about your injection experience?</td>
<td>To evaluate whether the application could possibly resolve that desire.</td>
</tr>
</tbody>
</table>

Table 1.: Pre-Trial Questionnaire
<table>
<thead>
<tr>
<th>Question</th>
<th>Reasoning</th>
</tr>
</thead>
<tbody>
<tr>
<td>Do you have Multiple Sclerosis?</td>
<td>To establish how relevant the application is to the participant.</td>
</tr>
<tr>
<td>After using the application, evaluate your experience in terms of injection anxiety.</td>
<td>To evaluate the user’s degree of injection anxiety and determine the application’s contribution in that regard.</td>
</tr>
<tr>
<td>How would describe your perceived pain while using the application?</td>
<td>To evaluate the user’s degree of perceived pain and determine the application’s contribution in that regard.</td>
</tr>
<tr>
<td>In terms of time, did the involvement of the app increase or decrease the injection duration?</td>
<td>To evaluate whether the app is beneficial or obstructing in terms of efficiency.</td>
</tr>
<tr>
<td>How would you rate the accuracy of the grid overlay?</td>
<td>To evaluate whether the grid overlay is suitable to the participant’s body.</td>
</tr>
<tr>
<td>How intuitive was it to position the grid on the injection area?</td>
<td>To evaluate the usability of the application with respect to the grid overlay.</td>
</tr>
<tr>
<td>Rate your overall experience with the features of the application.</td>
<td>To assess the overall usability of the application.</td>
</tr>
<tr>
<td>How would you go about improving the application?</td>
<td>To determine whether the application’s usability can be improved beyond what the developers anticipate.</td>
</tr>
</tbody>
</table>

Table 2.: Post-Trial Questionnaire

Example Instructions for thigh injection process

- Open the MSease application on your phone
- Select “Play” from the menu scene
- Select an Injection area from the Injection Sites scene
- Position yourself as you normally do for the corresponding injection
- Place the image target sticker on your knee.
- Aim at the image target with your phone’s camera (the overlay should then appear)
- Touch a blue tile on the screen where you need to complete the injection (the tile should then become pink)
- Put your finger on your thigh, at the exact location where the injection will be performed
- Put the phone down and grab the injection needle
- Perform the injection
- Put the needle away and grab your phone again
- Go back to the application menu and select “Journal”
- Go through the journal and consult the injection journal for relevant information.
- Go back to the application menu and select “Quit”

Upon completion of the above steps, the participants were asked to answer a post-experience questionnaire that focused on the change in perceived pain and injection anxiety, as well as the general features of the application. This questionnaire was comprised of the questions in Table 2.
5. Results

In the following section, we summarize the results of our two preliminary studies.

5.1. MS Patient Study

The results of our study with the MS participant contain data from two phases: the pre-trial and the post-trial. In the pre-trial phase, our participant was asked to describe the medication administration process using the standard tools given to them by their physician i.e. a simple paper-based MS journal. During this phase, the participant recorded their perceived levels of pain and injection anxiety during the administration of each dose of medication. In the post-trial phase, the participant was asked the same questions in order to gauge how effective our application was at alleviating their injection anxiety and perceived pain (see Table 3).

In our post-study interview with our MS patient, they expressed that while their experience with the application helped to significantly reduce their injection anxiety their perceived pain only reduced in the moment but did not decrease in the same way, since the injection itself remains a physically painful process.

5.2. MSease App Evaluation

In terms of overall user experience and interface design, the features of the application were well received by participants, regardless if they had MS or not. Table 4 demonstrates high ratings, averaging 4.3, for the appeal of the application. It can be said from these results that MSease satisfies desirability, accessibility, usability, and usefulness.

Furthermore, we asked all 14 participants as well as our MS patient about the ease of positioning the grid, the accuracy, and the possibility of increasing the efficiency of a needle injection process. These were all rated highly by all participants in the study.

<table>
<thead>
<tr>
<th>Application Feature</th>
<th>Average Value (1 to 5 scale)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall Aesthetic</td>
<td>5</td>
</tr>
<tr>
<td>Mascot</td>
<td>4</td>
</tr>
<tr>
<td>Overlay Quality</td>
<td>4</td>
</tr>
<tr>
<td>Menu</td>
<td>5</td>
</tr>
<tr>
<td>Calendar</td>
<td>5</td>
</tr>
<tr>
<td>Music</td>
<td>3</td>
</tr>
</tbody>
</table>

Table 3.: Summary of Injection Anxiety and Perceived Pain Responses

<table>
<thead>
<tr>
<th>Application Feature</th>
<th>Average Value (1 to 5 scale)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall Aesthetic</td>
<td>5</td>
</tr>
<tr>
<td>Mascot</td>
<td>4</td>
</tr>
<tr>
<td>Overlay Quality</td>
<td>4</td>
</tr>
<tr>
<td>Menu</td>
<td>5</td>
</tr>
<tr>
<td>Calendar</td>
<td>5</td>
</tr>
<tr>
<td>Music</td>
<td>3</td>
</tr>
</tbody>
</table>

Table 4.: Summary of responses regarding the general application features
6. Discussion

The results regarding injection anxiety and perceived pain indicate a reduction in both injection anxiety and perceived pain when using the AR application over the standard journal. These results show that a modern approach to MS treatment that incorporates new technologies like AR can have a positive impact on the medication administration process.

Similar to Schneider et al.'s study on the effectiveness of using virtual reality as a means of distraction during symptoms of distress during chemotherapy (8), we can also gather from our results that an XR application may indeed have potential to reduce stress levels during certain medical treatments (8). However, it is not fully well shown to what extent guided imagery can reduce the perceived pain of a patient. Although our MS patient has reported a slight decrease in perceived pain after using the MSease App, it may not be the case that it makes a significant difference with the pain all the time. On the other hand, we can confirm that guided imagery can have a positive impact on patients’ treatment anxiety, as discussed in Turners et al.’s study (9). To understand the extent to which this is the case, a larger study is needed and would make our results more conclusive.

6.1. Limitations of the MSease Application

A number of MSease’s features are not yet fully implemented considering that the application is still at a prototype stage. The limitations were disclosed to the participants while conducting the study. First of all, at the time of the study only one mascot was available to help reduce injection anxiety although the mascot should allow for customization in case some patients would prefer a different mascot that might further alleviate their stress and anxiety. For now, the overlay relies on an image target for placement of the grid, but optimally it should be generated by simply recognizing the body surface itself, this is a feature we are currently working on. The reminder feature has also yet to be implemented, thus patients need to keep track of their injection schedule with no assistance from the application. Lastly, patients can consult the journal section but cannot fully interact with it. For example, it is presently impossible to tap on an injection area and consult its history of injections. These features will be added in the next version of the application and studied with a larger population.
7. Conclusion

The aim of this project was to determine whether an AR-based MS journaling and injection application would be better than standard paper-based MS journals at alleviating injection anxiety and perceived pain during the administration of patients’ medication. To evaluate the effectiveness of an AR-based MS journal we had an MS patient compare their injection anxiety and perceived pain using both a standard journal and an AR journal. In order to perform this study, we developed an AR application in Unity containing three main parts: a grid for the injection sites, a mascot to help with guided imagery, and a journal to keep track of information related to injections. Users overlay the grid on top of the area of their body they wish to perform an injection on using the camera in their phone. Once positioned properly, users can identify available injection sites by the color of the squares in the grid. The mascot is included near the grid to help reduce the stress of the injection process. The journal replicates all of the required information from the physical version in electronic form. The results of our study begin to suggest that incorporating modern technologies in the treatment of people with MS can help to improve the overall experience by eliminating stressful elements like manual record-keeping and by making the process more soothing with pleasant visuals. However, it is important to note that although the interface was evaluated with a cohort of 15 participants, the results on injection anxiety and perceived pain are very preliminary as they come from a single MS patient, although one that has both anxiety and pain. In future work, we will expand our research sample size by involving a greater number of MS patients for more conclusive results. There is room for improvement for the current prototype in terms of the AR grid overlay aspect; instead of using Vuforia and an image target, we believe using OpenCV and machine learning for limb and body part recognition would make the placement of the overlay more accurate. This would entail collecting positive data (accepted thighs, arms, buttocks, and abdomen images) and negative data (anything that is not an accepted image of a limb or body part). Based on the previous literature and our preliminary studies we believe that mobile AR applications may help empower patients in other medication self-management domains such as insulin injections for people with diabetes.
References


