VirtualMindTrial: Virtual Clinical Trials for Mental Healthcare

Yugyung Lee  
Univ. of Missouri, KC  
leeyu@umkc.edu

Nikhilesh Katakam  
Univ. of Missouri, KC  
nkkc7@mail.umkc.edu

Deendayal Dinakarpandian  
Univ. of Missouri, KC  
dinakard@umkc.edu

Dennis Owens  
MPRG, KS  
owensd@sbcglobal.net

Abstract

The recruitment of human subjects for clinical trials research is a critically important step in the discovery of new cures for diseases. However, the current major recruitment methodologies are inherently inefficient. Virtual worlds such as Second Life\(^1\) have great potential to help improve the clinical trial recruitment process and overcome some of the limitations. The VirtualMindTrial system is developed through Second Life as an alternative to the traditional recruitment model for clinical trials. The VirtualMindTrial system offers a simulation of clinical trials workflow and can educate potential participants with visualization of the processes involved. We believe such systems are particularly valuable in increasing self-enrollment of sufficient numbers of patient volunteers and enhancing recruitment for clinical trial studies for development of new drugs.

1. Introduction

The recruitment of human subjects for clinical trials research is a critically important step in the discovery of new cures for diseases. Recruitment via the traditional methods of phone-based and face-to-face interviews is inefficient. This is one of the factors resulting in the high recruitment cost of clinical trials. There is considerable scope for improving on the current paradigm for recruiting. Ideally, one should be able to eliminate unsuitable patients or volunteers before initiating expensive screening and evaluation. However, this is often discovered only after considerable time and effort have been invested by both volunteer subject and clinical trial personnel. Recruitment for mental health research studies represents an additional challenge because afflicted subjects might be socially withdrawn and have a tendency to avoid direct human interaction. We envision virtual worlds as having great potential for improving the clinical trial recruitment process by overcoming several of its limitations [1]. Virtual worlds represent an exciting and emerging frontier that make it possible to create virtual objects, actors, and environments where information can be virtually exchanged and processed. The underlying technology makes it possible to transcend the physical barriers of space and time. The simulation of the clinical trial process using these technologies can also be useful in training and educating people involved in clinical trials. In the future, experiences of virtual clinical systems could be seamlessly integrated with the real clinical trial experiences.

We have developed a prototype virtual online system, called VirtualMindTrial, which enhances the efficiency and quality of recruitment of patients with psychiatric disorders for clinical research. The VirtualMindTrial system interacts virtually with potential subjects, but also provides research practitioners the ability to interact with subjects involved in clinical trials. As a first step towards validating the system, the initial version of the system has been implemented with a case study of clinical trials for Generalized Anxiety Disorder (GAD).

The remainder of the paper is organized as follows: Section 2 introduces related work on clinical trials and the use of virtual reality techniques in the medical domain. Section 3 presents the proposed system for virtual clinical trials. Section 4 discusses strengths and limitations. Section 5 concludes this paper.

2. Related work

Mental illnesses rank as one of the most common disease category in which volunteers for clinical trials express interest. Generalized Anxiety Disorder (GAD) is a well-characterized psychiatric disorder defined by excessive anxiety and worry for a period of at least six months. This common disorder is found in children as well as adults. A search on the US Clinical Trials

\(^{1}\) http://secondlife.com/
website retrieved 734 studies concerning Anxiety Disorders; it is an active area of clinical research.

There has been some progress in the standardization of different aspects of clinical trials – trial registry [2], trial authoring [3], and clinical guidelines [4]. There is a major ongoing effort in standardizing the BRIDG model for clinical trials. The Volunteer for Vanderbilt Research Program [5] is a good illustration of the benefits of using even a basic website for volunteer initiated recruitment. TrialX [6] is one of the more advanced online trial search systems based on semantic matching of trials with personal health records. Fink et al. [7] introduced an interactive web-based system which helps physicians in finding cancer patients and match them to relevant clinical trials. The interface helps clinicians to add new clinical trials and appropriate selection criteria for each trial, thereby providing means to extend their knowledgebase. Embi et al. [8] present a clinical trial alert system which notifies the physician when it finds an eligible patient for an ongoing clinical trial.

Virtual worlds go a step beyond web-based systems in offering an immersive and informative personalized experience, with the option to be anonymous. Virtual world platforms such as Second Life have been used in health care. The IBM’s Virtual health care island [9] is a futuristic representation of the challenges and opportunities facing today’s health care industry. It also shows how Information Technology can help in improving global health care delivery. The Plumbing Advise project [10] demonstrates a futuristic hospital environment equipped with various features such as Wi-Fi, Cisco real estate framework for health care and much more.

Medical Simulation in the Virtual World of Second Life by MUVers [11] simulates medical treatment procedures such as measuring the patient’s heart rate, intravenous administration and supplying oxygen. Second Life for E-Health - Laval 08 [12] aims at providing patients suffering with mental disorders integrated therapy with online support sessions. Game-based learning for Virtual Patients in Second Life [13] shows scenarios taking place in a day to day hospital environment. Patients get to learn medical procedures through games. 3D Emergency Preparedness Training [14] simulates various actions that people need to take in case of emergency. Some of the scenarios mentioned are calling emergency services in case of an accident.

3. Virtual clinical trials

The VirtualMindTrial system aims at the enhancement of the efficiency and quality of recruitment of patients with psychiatric disorders for clinical research (Figure 1). It not only allows recruiters to interface virtually with potential volunteers, but also offers a unique way for interested but busy and research naïve practices the opportunity for their patients to learn about and perhaps eventually participate in clinical trials. The key features of the system and the consequent advantages are summarized as follows:

**Virtual Recruiting:** Groups of potential volunteers with expressed interest in being notified about an opportunity for participating in a virtual clinical trial session for which they might qualify are characterized in a manner which facilitates matching with appropriate trials.

**Automated Screening and Medical Checkup:** Ease and speed of compilation of relevant screening and medical checkup for potential volunteer and subjects for clinical trials research. This allows a broader population reach with virtual communities and can be potentially global.

**Multi-modal and Multimedia based Interaction:** Some of the interactions between participants and systems are based on human gestures where they are used to automatically control the applications of the virtual recruitment system. Virtual chatting and video conferencing features connecting virtual and real worlds allow participants to have more realistic interactions and experiences.

**Intelligent Screening:** This needs appropriately selected questionnaires based on advanced analysis of inclusion and exclusion criteria. The system provides an intuitive and intelligent screening process with questionnaires that are carefully designed by criteria analysis from diverse sources. This facilitates rapid and accurate assessment of suitability for clinical trials.

**Educational Interface:** Providing effective education and training on clinical trials research to volunteer subject and clinical trial personnel in an immersive manner.

**Virtual Community:** Opportunity for participants and potential volunteers to share their experiences and knowledge on clinical trials research through an interactive forum, thus building a virtual clinical trial community.

---

2 www.clinicaltrial.org (Accessed date: Mar 14, 2010)
3.1. VirtualMindTrial system

The objectives of the VirtualMindTrial system are (1) To provide an easy and innovative way for inviting, educating and recruiting a patient for a clinical trial study and (2) To monitor participant health on a regular basis after being assigned to a particular study. The architecture of the VirtualMindTrial system provides a virtual interface for clinical trials research with multiple participants such as patients/volunteers and recruiters. It dynamically maps a personalized interface to prospective users depending on their roles and responsibilities. For patients and volunteers, it facilitates proactive recruitment registration and helps recruiters to review comprehensive recruitment status including the number of contacts made, associated demographic information and the number of qualified/disqualified participants for a given study. For physician and researchers, it supports the design of eligibility criteria and questionnaires per protocol and updates existing questions.

3.1.1. Patient manager. The online screening interface is based on a well defined patient model consisting of demographic information including educational, occupational, socioeconomic and residential information. It can

- Demonstrate that the information provided has been regularly refreshed
- Provide automated and personalized follow-up with both the patient and recruiters
- Provide online registration that is interactive and personalized
- Screen, evaluate, and report results
- Prompt patients regarding follow-up

3.1.2. Recruiter manager. The interface aids recruiters in searching for qualified patients/volunteers for a particular study, reviewing a comprehensive report of recruitment status including the number of qualified/disqualified participants for a study. It can

- Generate a list of potential patients in response to a query containing inclusion/exclusion criteria for a particular study
- Automatically forward information on subjects matching study criteria so that they may be contacted by the appropriate clinical trial team
- Integrate data from heterogeneous data sources and carry out real time data analysis
- Provide data indicating the efficiency of recruitment with information on cost savings
- Determine most appropriate sites for a given study based on the location of potential patients

3.1.3. Physician/Research manager. Clinical research personnel can view the questionnaires for a clinical study, update existing criteria or questions, and publish new criteria or questions through the online interface to the question database.

The virtual system can be used to educate users about the clinical trial process, provide means to the patient willing to participate in clinical trials, and provide means for the recruiters to monitor the health information of enrollees. An important focus is to connect virtual world environment (Objects and Avatars) with concepts and persons in the real world.

The features of virtual clinical trials for mental healthcare are:

- Sending invitation to avatars (i.e., patients/healthy volunteers) for participating in a clinical trial study.
- Educating participants about clinical trials through presentations and videos.
- Registering patients/healthy volunteers for a clinical trial.
- Examining the eligibility of a patient/healthy volunteer for participating in a clinical trial study and assigning him/her to an ongoing study.

![Figure 1. Architecture of VirtualMindTrial](image-url)
Monitoring the participant’s health as part of the clinical trial process.
Follow up on participant’s health history.
Monitor population registration on a map.

3.2. Clinical trial invitation and education

3.2.1. Sending invitations. In real life, a Clinical Trial Research Organization (CRO) invites volunteers to participate in a particular clinical trial study by putting our advertisements. We simulate this process by using Second Life to identify a list of potential and invite them to join the virtual clinical trial group. The avatars can accept or decline the invitations. On acceptance, the avatars receive information about clinical trials via Second Life note cards. These note cards act as an invitation and spell out steps or procedures that a subject needs to follow in order to get registered for a clinical trial. Figure 2 shows the avatar getting a note card.

Figure 2. Avatar Receiving an Invitation

Patient and caregiver education is an important part of efforts for optimizing recruitment, retention and meeting the highest standards of informed consent. This is an ongoing process with the VirtualMindTrial system and over time should also lead to better compliance and knowledge of therapeutic options for patients and their families. A number of high-quality informational healthcare websites are available, but we do not fully utilize them for clinical trial education and training. This module is composed of interactive materials that illuminate the new drug development process including the benefits derived by society, the sine qua none participation of normal healthy and patient volunteers, a generic “walk-through” regarding what volunteers can expect when involved in clinical trials and a general discussion of risks and benefits. Specifically, educational material in multiple formats (text, animation, and video) shall be made available on the website to adapt to differing learning styles followed by a self-administered test to demonstrate comprehension of what participation in clinical trials in general and the VirtualMindTrial system in particular entails.

3.2.2. Educating patient’s about clinical trials. After the patient/volunteer receives a note card about virtual clinical trials, he/she visits the open registration center. Once they arrive at the open registration centers they educate themselves about clinical trials, by watching videos and presentations on a smart video screen and a slide viewer respectively. The interaction with these devices is gesture based, e.g., the user gently waves his hand to play video. A stop gesture is used to stop playback.

Here is a brief explanation for the implementation of the gesture based communication in second life. In second life we can make an avatar to perform a gesture (Pre-defined or Custom built gestures). Also associated to each gesture we can send a message on the chat client in second life on a specific port, i.e. whenever the gesture is performed by the avatar, a message goes simultaneously in the chat console. This is achieved using the llSay("Message", "port number") command. Now each object (for example the video screen) can listen to a specific message on a particular port number. This can be done using the llListen()
command. So the scenario is when we make a gesture, we are indirectly communicating on the chat client on a specified port and when an object listening on the port receives the message we perform a particular task. Table 1 gives the list of gestures that the users can use at the video screen. Figure 3 shows the avatar accessing videos with various gestures. Figure 4 shows the avatar using the slide viewer to view presentations on clinical trials.

Table 1: Gestures for Controlling a Video Screen

<table>
<thead>
<tr>
<th>Gesture</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wavehand</td>
<td>Plays the next available video on the video screen.</td>
</tr>
<tr>
<td>Point you</td>
<td>Resets the video screen</td>
</tr>
<tr>
<td>Touch</td>
<td>Shows the next slide on the presentation.</td>
</tr>
</tbody>
</table>

3.3. Virtual registration process

3.3.1. Personalized recruitment. This is based on intelligent processing in the selection of appropriate strategies for recruitment, at either the level of a trial or for individual subjects. Ideally, each subject interacting with the system should have a personalized and optimized experience. For instance, some might prefer a graphical interface and others a textual/chart interface; some might prefer Spanish to English. Some, while wishing to participate in clinical trials, may not have the patience to complete detailed questionnaires. It might be a better strategy to obtain minimal information by dynamically switching to an abbreviated questionnaire that still gathers useful input. In turn, questionnaire modules that are either left incomplete or marked in an inconsistent fashion might point to a need to redesign the questionnaire. This level of dynamic optimization is achievable by the meticulous compilation of statistics, not just on subject data, but also interaction patterns of potential subjects with the system. The accruing data can subsequently be mined by algorithms to improve the overall effectiveness of the clinical trial recruitment process. For example, the system will have the capacity to learn from negative “dropout” and positive “stick-with-it” cases.

3.3.2. Registering for a clinical trial. The virtual registration process has been made very easy using a smart magic watch that is attached to the avatar’s right hand to transmit the avatar’s information using a specified channel. Figure 5 shows a screen shot of the smart magic watch transmitter. This transmitter transmits the avatar information such as name, height, weight, age, gender; phone no, blood pressure, heart rate, and sugar level.

When an avatar approaches the registration screen, a message is sent from the transmitter to the smart registration screen via a specified channel. Upon receiving the required information the smart registration interface registers the avatar in the system. When an avatar subsequently approaches the registration, it takes his/her information from the transmitter and checks whether he/she has already registered or not. If he/she is already registered, then his/her registration details are displayed on the screen along with a message. In addition, the smart registration screen sends an SMS to the patient’s mobile phone number (Figure 6).
3.4. Virtual questionnaire and monitoring

A general set of introductory questions common to all volunteers contains a subset of disease-specific probing questions which launch appropriate sets of detailed questions. These are based on standard criteria like those in the “Diagnostic and Statistical Manual of Mental Disorders (DSM-IV).” The generation of the questionnaire is interactive to ensure that i) questions are not redundant and ii) sufficient details are elicited based on the specific medical background of the volunteer. General questions cover basic demographic information (e.g., name, address), medical corroboration information (e.g., names of psychiatrists, physicians and facilities visited, past tests performed), trigger questions to suggest detailed questionnaires to be used (e.g., known diagnoses, history of suicidal behavior), and questions related to consent for being contacted and/or access to clinical records.

Appropriate disease-specific questions are triggered based on the responses to the general questionnaire. These are framed as checklists and multiple choice questions with the aim of capturing a rich amount of detail without resorting to free text input. Further, this allows the detection of inconsistencies in volunteer responses to reduce the probability of having the system corrupted by spurious data. Volunteer responses can be mapped to Clinical Trial databases to validate the eligibility for participating in a clinical study. In addition, the online administration of well-validated psychometric testing can be performed. These would be routinely and frequently administered to samples of the given group and therefore provide a statistically-reliable measure of psychometric characteristics of the diagnostic group populating the database at any given time point.

3.4.1. Edibility Test. At this stage of recruitment, we need to examine the eligibility of a patient/volunteer for participating in a clinical trial study and assigning him/her to an ongoing study. After successfully registering with the system the patient approaches the live test screen located at the examination center. The interactive quiz session is designed to help a recruiter find whether the patient/volunteer is eligible for an ongoing trial. Figure 7 shows the live test screen. The user interacts with this screen with the gestures shown in Table 2.

<table>
<thead>
<tr>
<th>Gesture</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>Posts an “yes” answer to the question</td>
</tr>
<tr>
<td>No</td>
<td>Posts an “no” answer to the question</td>
</tr>
<tr>
<td>Hey</td>
<td>Starts the test</td>
</tr>
<tr>
<td>Point you</td>
<td>Reset the test screen</td>
</tr>
</tbody>
</table>

Alternatively the patient/volunteer can take a test by interacting with a live recruiter through a video chat session as shown in Figure 8.

3.4.2. Monitoring patient’s health. Various tests such as blood pressure, heart rate and blood sugar level are routinely administered. After the checkup test in the above step, when the patient approaches the recruiter (bot [15]), the lab monitor displays graphical results of the patient’s heart rate, blood pressure, and sugar level. Figure 9 shows how these values are recorded and displayed on a screen to users. The simulated Lab room helps patient to take various tests, and is equipped with various devices as shown in Figure 10 and the test results are shown in Figure 11.
3.4.3. Displaying registration summary on maps. Adequate geographical coverage is often an important planning and targeting recruitment for the success of a clinical trial. Recruiters can monitor the extent and distribution of patient registration by a map view, which displays the total number of registrations on a map interface (Figure 12).

3.5. System implementation

The VirtualMindTrial system is implemented as Web services with Microsoft SQL on the .NET Platform. Web Services are widely used to develop Service oriented architecture (SOA) based systems that allows us to benefit from dynamic discovery, selection and composition of Web Services [16]. We have implemented several new Web Services in addition to using existing Web Services such as GoogleMaps and Microsoft chat controls. For security, the user authentication and role-based registration discussed in Section 3 is implemented. Additional components provide for frequent updating of the knowledge base for the eligibility of clinical trial studies and ensure that industry IT security and the Health Insurance Portability and Accountability Act (HIPAA) confidentiality standards are met. Specifically, informed consent of participants needs to be obtained and subject confidentiality maintained.

The VirtualMindTrial system is designed using client-server architecture (Figure 1) that includes: 1) A server for handling various Web services including registration service, education service, invitation service, screening and lab test services, visualization service and 2) Second Life as a client for visualization of the clinical trials. Our implementation is described in detail in Appendix. The sequence diagram of the VirtualMindTrial system is shown in Figure 13. The web services used for the server have been developed using Asp.net and C#. All the pages, service and videos sources are hosted at the VirtualMindTrial site [17]. In the client implementation, Second Life Linden Scripting language is used for interacting with Second Life objects and avatars. The Linden Script built-in functions are used to manipulate SL objects including avatar attachments. In addition, we use Metaverse technology to control the objects by automated Viewers, called "bots" (a contraction of "robot"). This allows for the creation of custom Viewers that can log in without a human operator and perform the same actions as any normal avatar in the world. The Second Life Client of the VirtualMindTrial system is available at [18]. The project video is also available at [19].
4. Discussion

Compared to existing online systems like the Vanderbilt Program and the Interactive Autism Network (IAN), the VirtualMindTrial system is a sophisticated approach that offers unique advantages to enhance the efficiency of recruitment and conduct of clinical trials. We believe that virtual worlds such as Second Life have great potential to help improve the clinical trial recruitment process and are particularly valuable in self-enrollment of sufficient numbers of patient volunteers and recruitment for clinical trial studies for development of new drugs. The virtual and online nature and personalized interface of the system will facilitate recruitment and retention of populations which may be geographically disparate and/or socially withdrawn. Since our system is implemented in a service fashion, customized to each individual, and also fully simulated and visualized in a virtual world, we expect that most volunteers will find it a relatively pleasant experience. From the technical perspective, there are certain limitations with Second Life technologies. The most important limitation is the limited set of functions offered by Linden Scripting language. Although SL viewer 2 has brought significant media functions, a lot of effort is needed to connect virtual worlds with real worlds. We anticipate that virtual world environments will grow in scope to offer a seamless connection with the real world.

5. Conclusion and future work

In this paper, we presented the VirtualMindTrial system to demonstrate how Virtual World technologies can be used to improve clinical trial recruitment process. We believe that Virtual Worlds such as Second Life have great potential to improve the clinical trial experience both from an economic and human viewpoint. We also believe that potential subjects will find this system to be of use in determining the feasibility, design and execution of trials, based on the availability of populations likely to meet inclusion/exclusion criteria. The virtual process of clinical research can offer an immersive experience with an emphasis on patient education and the informed consent process, in contrast to the current paradigm which is heavily dependent upon mass media advertising typically performed ad hoc as the need to recruit for a new study arises.

In the future, the following features will be addressed: 1) Dynamically transmitting patient details from a real world environment into Second Life, 2) Making use of Second Life voice APIs to connect a mobile phone in a real world and 3) Using two way screening protocols to improve the interaction between recruiters and avatar.

6. Acknowledgements

We could like to acknowledge Dr. Wubbenhorst John of Midwest Psychiatric Research Group for discussions on the project and the National Institute Health for funding the project (1R43MH085372-01A1).

7. References

Appendix: Implementation Description

Web services (Methods):
public string GetQuestion(string questionno) :  
  Input : Question number
  Output : string
public string NewRegisterPatientsMethod(string name, string age, string height, string weight, string gender, string phoneno) :  
  Input : name, age, height, weight, gender, phonenumber
  Output : string
public bool IsAlreadyRegistered(string name) :  
  Input : patient name
  Output : bool
public Hashtable GetPatientDetails(string name) :  
  Input : Patient name
  Output: Hashtable of patient details
public string GetPatientId(string name) :  
  Input : Patient name
  Output: Patient id
public bool ValidateUser(string registrationNo) :  
  Input : Registration number
  Output: bool
public bool AssignPatientToAStudy(string study, string registrationNo) :  
  Input : Registration number, study
  Output: string
public bool DidPatientPassTheTest(string id) :  
  Input : patient id
  Output: bool

Applications:
Ustream : To broadcast the recruiter web came on a live stream (Livestream.aspx)
Google charts : used on patient health monitor and patient lab results monitor (patienthealthmonitor.aspx, labresults.aspx)
Google map charts : To display patient population in each state (patientpopulation.aspx)

Metaverse APIs Methods for Bot:
client.Self.Chat(): To chat with the avatar in the Second Life.
client.Appearance.SetPreviousAppearance(): To set the bots appearance

Important Methods and LL functions:
llEmail(): To send email from Second Life environment . I have used this method to send SMS.
llParcelMediaCommandList() : Used to set the parcel media properties
llListen(): Used to listen for an appropriate message on a specified channel
llSay(): Use for communication between object on a specified channel
llGiveInventory(): To give away notecards
llRequestAgentData(): To retrieve avatars name, DOB
llGetAgentSize(): To get the agent size.
OLEDBConnection : to connect to the Access Database
OLEDBCommand : to specify the SQL Query
Execute NONquery(): Used to insert values into the database.
Execute scalar(): to retrieve a single column value.

Linden Script for Video Screen Scenario
default
{ state_entry()
  { listen_handle = llListen(402, "", llGetOwner(), "");
    listen_handle1 = llListen(403, "", llGetOwner(), "");
  }
  listen(integer channel, string name, key id, string message )
  { if(channel == 402)
    { if(count==1)
    // Side to display the media on.
      {integer a= llSelPrimMediaParams(4,
    // Show this page immediately
    [PRIM_MEDIA_AUTO_PLAY,TRUE,
      // The URL currently showing
      PRIM_MEDIA_CURRENT_URL,"http://www.youtube.com/watch?v=dRmBJhtys9g&autoplay=1&fs=1",
      // The URL if they hit 'home'
      PRIM_MEDIA_HOME_URL,"http://www.youtube.com/watch?v=dRmBJhtys9g&autoplay=1&fs=1"
    ]);
      count = count +1; // rounded up to nearest power of 2.
    }
    ...}
Figure 13. Sequence Diagram for Video Chat Session of the VirtualMindTrial System